

=> fil lreg

FILE 'LREGISTRY' ENTERED AT 11:47:39 ON 30 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 1985 AMERICAN CHEMICAL SOCIETY (ACS)

LREGISTRY IS A STATIC LEARNING FILE

=> fil reg

FILE 'REGISTRY' ENTERED AT 11:47:41 ON 30 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 28 NOV 2004 HIGHEST RN 790189-55-8
DICTIONARY FILE UPDATES: 28 NOV 2004 HIGHEST RN 790189-55-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> fil marpat

FILE 'MARPAT' ENTERED AT 11:47:44 ON 30 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

FILE CONTENT: 1988-PRESENT (VOL 141 ISS 22) (20041126/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	6800776	05 OCT 2004
DE	10314780	30 SEP 2004
EP	1464371	06 OCT 2004
JP	2004260057	16 SEP 2004
WO	2004087649	14 OCT 2004

Structure search limits have been raised. See HELP SLIMIT for the new,
higher limits.

=> fil hcap

FILE 'HCAPPLUS' ENTERED AT 11:47:47 ON 30 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 30 Nov 2004 VOL 141 ISS 23
FILE LAST UPDATED: 28 Nov 2004 (20041128/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

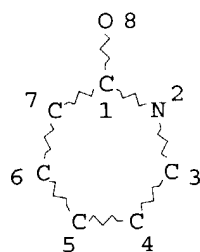
=> file stnguide

FILE 'STNGUIDE' ENTERED AT
USE IS SUBJECT TO THE TERMS
COPYRIGHT (C) 2004 AMERICAN
AND TECHNOLOGY CORPORATION,

FILE CONTAINS CURRENT INFOR
LAST RELOADED: Nov 26, 2004

=> d que 121

L1 STR



NODE ATTRIBUTES:

CONNECT IS E1 RC AT 8
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE

L2 3008 SEA FILE=MARPAT SSS FUL L1
L13 3008 SEA FILE=HCAPLUS ABB=ON PLU=ON L2
L14 15819 SEA FILE=HCAPLUS ABB=ON PLU=ON ?METALLOPROTEAS? OR MMP?
L15 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND L14
L16 1441184 SEA FILE=HCAPLUS ABB=ON PLU=ON ?MERCAPT? OR ?THIO? OR
?SULFENYL? OR ?CYSTYL? OR ?CYSTEIN? OR ?SULFAN? OR ?SULFID?
L17 1073 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND L16

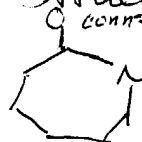
Marpat - based search

L1: STR to search in Marpat

L2: Search in Marpat

L13: Retrieve corresponding HCAPLUS records

• all of these hits have at least one Markush structure containing



L15-L17: limit w/ text

L18 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND L17
L21 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR L15

=> d iall hitstr l21

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

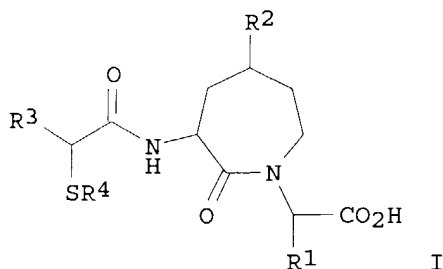
L21 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:625347 HCAPLUS
DOCUMENT NUMBER: 141:157040
ENTRY DATE: Entered STN: 04 Aug 2004
TITLE: 1-carboxylmethyl-2-oxo-3-acylaminoazepans useful as
selective inhibitors of MMP-12 matrix
metalloproteinase
INVENTOR(S): Warshawsky, Alan M.; Janusz, Michael J.
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: U.S., 29 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D223-12
SECONDARY: C07D401-00; C07D405-00; C07D409-00; A61K031-55
US PATENT CLASSIF.: 514212030; 514212080; 540524000; 540527000
CLASSIFICATION: 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6770640	B1	20040803	US 1999-467292	19991217
PRIORITY APPLN. INFO.:			US 1998-155205P	P 19981231

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6770640	ICM	C07D223-12
	ICS	C07D401-00; C07D405-00; C07D409-00; A61K031-55
	NCL	514212030; 514212080; 540524000; 540527000
US 6770640	ECLA	C07D223/12; C07D403/12+223+209

OTHER SOURCE(S): MARPAT 141:157040
GRAPHIC IMAGE:



ABSTRACT:

Title compds. [I; R1 = H, alkyl, CH₂SCH₂NHAc, (CH₂)pA, (CH₂)mB, CHDR7; A = aryl, heteroaryl, cyclohexyl; B = N(R7)₂, guanidino, nitroguanidino, CO₂R6, CONR6; D = O, S; R2 = alkyl, (CH₂)pheteroaryl, (CH₂)pAr; Ar = (substituted) Ph, naphthyl; R3 = W(CH₂)m, QZ(CH₂)m; W = phthalimido; Q = H, Y(CH₂)n; Z = O, NR6, CONR6, SO₂NR6, etc.; Y = H, aryl, heteroaryl, CO₂R6, N(R6)₂, morpholino, piperidino, pyrrolidino, isoindolyl; R4 = H, COR7, CO(CH₂)qK, SG; G = pyridinyl(alkyl), azolylalkyl, phenylalkyl, etc.; K = morpholino, piperidino, pyrrolidino, imidazolyl, pyridinyl, etc.; R6 = H, alkyl; R7 = H, alkyl, (CH₂)pAr; m = 2-4; n = 0-4; p = 0-2], were claimed (no synthetic or biol. data).

SUPPL. TERM: carboxylmethyloxyacylaminoazepan **MMP12** matrix metalloproteinase inhibitor; emphysema smoking induced treatment azepan carboxymethyl oxo acylamino

INDEX TERM: Drug delivery systems
Human
(1-carboxylmethyl-2-oxo-3-acylaminoazepans useful as selective inhibitors of **MMP-12** matrix metalloproteinase)

INDEX TERM: Emphysema
(treatment of smoking induced emphysema; 1-carboxylmethyl-2-oxo-3-acylaminoazepans useful as selective inhibitors of **MMP-12** matrix metalloproteinase)

INDEX TERM: 9004-06-2, **MMP 12**
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(**MMP-12** inhibitors; 1-carboxylmethyl-2-oxo-3-acylaminoazepans useful as selective inhibitors of **MMP-12** matrix metalloproteinase)

INDEX TERM: 60-32-2, 6-Aminohexanoic acid 15100-75-1,
(S)-Phenylalanine tert-butyl ester hydrochloride 90719-32-7, (S)-4-Benzyl-2-oxazolidinone 143365-54-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(carboxylmethylacylaminoazepanones useful as selective inhibitors of **MMP-12** matrix metalloproteinase)

INDEX TERM: 4443-26-9P, 6-Phthalimidohexanoic acid 5107-16-4P
205391-14-6P 205391-15-7P 205391-16-8P 205391-17-9P
205391-18-0P 205391-19-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(carboxylmethylacylaminoazepanones useful as selective inhibitors of **MMP-12** matrix metalloproteinase)

INDEX TERM: 731851-42-6P 731851-43-7P 731851-44-8P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(carboxylmethylacylaminoazepanones useful as selective inhibitors of **MMP-12** matrix metalloproteinase)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Anon; EP 0726072 1996 HCAPLUS
(2) Anon; EP 0599444 1998 HCAPLUS
(3) Anon; WO 9812211 1998 HCAPLUS
(4) Anon; WO 9935145 1999 HCAPLUS
(5) Karanewsky; US 5552397 A 1996 HCAPLUS
(6) Neustadt; US 5075302 A 1991 HCAPLUS
(7) Robl; US 5654294 A 1997 HCAPLUS
(8) Robl; US 5856476 A 1999 HCAPLUS
(9) Robl; J Am Chem Soc 1994, V116, P2348 HCAPLUS

- (10) Robl; J Med Chem 1996, V39, P494 HCAPLUS
 (11) Robl; Tetrahedron Lett 1994, V35(9), P1393 HCAPLUS
 (12) Robl; Tetrahedron Lett 1996, V37(50), P8985 HCAPLUS
 (13) Warshawsky; Bioorg Med Chem Lett 1996, V6(8), P957 HCAPLUS

=>

=> d ibib abs ed hitind hitstr retable l21 2

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L21 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:569862 HCAPLUS

DOCUMENT NUMBER: 141:123901

TITLE: Preparation of N-sulfonyl-cyclic amine-2-carbohydroxamic acid derivatives as **metalloprotease** inhibitors

INVENTOR(S): Natchus, Michael George; De, Biswanath; Pikul, Stanislaw; Almstead, Neil Gregory; Bookland, Roger Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 186,531.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

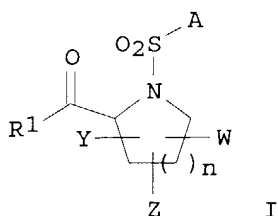
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138260	A1	20040715	US 2003-730572	20031208
US 6417219	B1	20020709	US 1997-918317	19970826
US 2002061877	A1	20020523	US 2001-888675	20010625
US 6569855	B2	20030527		
US 2002072517	A1	20020613	US 2001-888759	20010625
US 2003105153	A1	20030605	US 2002-186531	20020701
US 2003191163	A1	20031009	US 2002-308780	20021203
JP 2004115531	A2	20040415	JP 2003-384116	20031113
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			US 1997-918317	A3 19970826
			US 2001-888675	A2 20010625
			US 2001-888759	B2 20010625
			US 2002-186531	A2 20020701
			JP 1998-511715	A3 19970822

OTHER SOURCE(S): MARPAT 141:123901

GI



AB The invention provides compds. according to formula (I), in particular N-sulfonylpyrrolidine-2-carbohydroxamic acid derivs., [wherein A = each (un)substituted alkyl, heteroalkyl, aryl, or heteroaryl; R1 = NHOR2 (where R2 = H, alkyl); W = one or more of H, lower alkyl, or an alkylene bridge that forms a ring in addition to the main ring; Y = independently one or more of HO, SR3, SOR4, SO2R8, alkoxy, or (un)substituted amino (where R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino); Z = H, HO, or alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the main ring; n = 1; some provisos applied], pharmaceutically-acceptable salts, biohydrolyzable amides, esters, or imides thereof are prepared. These compds. are useful as inhibitors of **metalloproteases**, and effective in treating conditions characterized by excess activity of these enzymes, in particular restenosis. Thus, cis-hydroxy-D-propine was condensed with 4-methylphenylsulfonyl chloride in the presence of Et3N and 2,6-dimethylpyridine in aqueous dioxane at room temperature for 14 h gave N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine which was esterified with MeOH and SOCl2 to give N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine Me ester which was treated with hydroxylamine monopotassium salt in MeOH overnight to give (2R,4S)-1-(4-Methoxyphenylsulfonyl)-2-(N-hydroxycarboxamido)-4S-hydroxypyrrolidine.

ED Entered STN: 16 Jul 2004

IC ICM A61K031-445
ICS A61K031-454; A61K031-4025; A61K031-4015

NCL 514317000; 514326000; 514422000; 514423000

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7

ST restenosis treatment phenylsulfonylpyrrolidinecarbohydroxamic acid prepn;
phenylsulfonylpyrrolidinecarbohydroxamic acid prepn
metalloprotease inhibitor; sulfonyl cyclic amine carbohydroxamic acid prepn **metalloprotease** inhibitor

IT Amines, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as **metalloprotease** inhibitors for treatment of restenosis)

IT Human
(preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as **metalloprotease** inhibitors for treatment of restenosis)

IT Artery, disease
(restenosis; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as **metalloprotease** inhibitors for treatment of restenosis)

IT 1138-54-1P, 4-(Isobutoxy)phenylsulfonyl chloride 57850-07-4P,
1-(4-Methylphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 64700-65-8P, (2R)-2-Methoxycarbonyl-5-pyrrolidinone 182937-63-9P,
(2R)-2-Benzoyloxy-3-phenylpropanoic acid 203934-42-3P,
1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-4-oxopyrrolidine 203934-63-8P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 203994-66-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-(4R)-hydroxypyrrolidine 203994-80-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 203994-82-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-**acetylthiopyrrolidine** 204072-15-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-benzoyloxypyrrolidine 204072-16-2P,
1-(4-Methoxyphenylsulfonyl)-(2S)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-17-3P, 1-(4-Methoxyphenylsulfonyl)-(2S)-carbomethoxy-(4S)-hydroxypyrrolidine 204072-18-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-

carboxy-(4S)-hydroxypyrrolidine 204072-19-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-methoxypyrrolidine 204072-20-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-[(trifluoromethanesulfonyl)oxy]pyrrolidine 204072-21-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-benzothiazolylthio)pyrrolidine 204072-22-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-hydroxypyrrolidine 204072-23-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-(2-benzothiazolylthio)pyrrolidine 204072-24-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1-methyl-2-imidazolylthio)pyrrolidine 204072-25-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-(1-methyl-2-imidazolylthio)pyrrolidine 204072-26-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-phenoxy-pyrrolidine 204072-27-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[4-(benzyloxy)phenoxy]pyrrolidine 204072-28-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-phenylaminophenoxy)pyrrolidine 204072-29-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-pyridinyloxy)pyrrolidine 204072-30-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-phenylthiopyrrolidine 204072-32-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-methoxyphenylthio)pyrrolidine 204072-34-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-methoxyphenylthio)pyrrolidine 204072-36-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-ethoxymethoxypyrrolidine 204072-37-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-benzyloxymethoxypyrrolidine 204072-38-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-[(2-methoxyethoxy)methoxy]pyrrolidine 204072-39-9P 204072-40-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-4-oxopyrrolidine 204072-41-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-4-hydroxy-4-ethylpyrrolidine 204072-42-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-4-hydroxy-4-phenylpyrrolidine 204072-44-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-3,3-dimethyl-4-oxopyrrolidine 204072-45-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-3,3-dimethyl-(4R)-hydroxypyrrolidine 204072-46-8P, 1-(3,4-Dimethoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-47-9P, 1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-50-4P, 1-(4-Bromobenzenesulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-51-5P, 1-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-52-6P, 1-(2,4-Dichlorophenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-53-7P, 4-(2-Methoxyethoxy)phenylsulfonyl chloride 204072-56-0P, 1-(4-Isobutyloxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 204072-57-1P, 1-(2-Methyl-4-bromophenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-methoxyphenylthio)pyrrolidine 204072-58-2P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-benzothiazolylthio)pyrrolidine 204072-59-3P, 1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-benzothiazolylthio)pyrrolidine 204072-60-6P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-methoxyphenylthio)pyrrolidine 204072-61-7P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(3-pyridyloxy)pyrrolidine 204072-62-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-azidopyrrolidine 204072-63-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-aminopyrrolidine 204072-64-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-methylsulfonyloxypyrrolidine 204072-65-1P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-azidopyrrolidine 204072-66-2P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-aminopyrrolidine 204072-67-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-propylaminopyrrolidine

204072-68-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(hexylamino)pyrrolidine 204072-69-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(2-phenylethylamino)pyrrolidine 204072-70-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(N-butyl-N-hexylamino)pyrrolidine 204072-71-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(methanesulfonyl)amino]pyrrolidine 204072-72-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(methanesulfonyl)amino]pyrrolidine 204072-74-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(3-pyridylmethyl)amino]pyrrolidine 204072-75-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(3-pyridylmethyl)-N-(methanesulfonyl)amino]pyrrolidine 204072-76-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[bis(methanesulfonyl)amino]pyrrolidine 204072-77-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(methanesulfonyl)-N-propylamino]pyrrolidine 204072-78-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(4-methoxyphenylsulfonyl)amino]pyrrolidine 204072-79-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(hexanoylamino)pyrrolidine 204072-81-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(methylcarbamoyl)amino]pyrrolidine 204072-82-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxypropyl)amino]pyrrolidine 204072-83-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxy-3-phenylpropyl)amino]pyrrolidine 204072-84-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxypropyl)-N-propylamino]pyrrolidine 204072-85-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-hydroxypropyl)-N-propylamino]pyrrolidine 204072-86-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-benzyloxy-3-phenylpropyl)-N-propylamino]pyrrolidine 204072-87-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[N-(1-oxo-(2R)-hydroxy-3-phenylpropyl)-N-propylamino]pyrrolidine 204072-88-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1-piperidyl)pyrrolidine 204072-89-9P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1-piperidyl)pyrrolidine 204072-90-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(morpholino)pyrrolidine 204072-91-3P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(morpholino)pyrrolidine 204072-92-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1,1-dioxothiormorpholino)pyrrolidine 204072-93-5P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(1,1-dioxothiormorpholino)pyrrolidine 204072-94-6P 204072-95-7P 204072-96-8P 204072-97-9P 204072-98-0P 204072-99-1P 204073-00-7P 204073-04-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-4,4-bis(ethylthio)pyrrolidine 537704-28-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[4-(1,1,3,3-tetramethylbutyl)phenoxy]pyrrolidine 537704-32-8P, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-[(1-methyl-3-imidazolyl)sulfonyl]amino]pyrrolidine 537704-35-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-(4-biphenylamino)pyrrolidine 722550-48-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-(methanesulfonyl)pyrrolidine 722550-49-4P, 1-[4-(2-Methoxyethyl)phenylsulfonyl]-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine 722550-52-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-5-pyrrolidinone 722550-53-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-5-pyrrolidinone 722550-54-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-benzyloxycarboxamido)-5-pyrrolidinone

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reagent or reagent)

(intermediate; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as metalloprotease inhibitors for treatment of restenosis)

IT 81669-70-7, Metalloprotease

RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (preparation of N-sulfonyl pyrrolidine-2-carboxylic acid as **metalloprotease** inhibitors for treatment of restenosis)
- IT 204072-55-9P, 1-(4-Phenoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of N-sulfonyl pyrrolidine-2-carboxylic acid as **metalloprotease** inhibitors for treatment of restenosis)
- IT 204071-36-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-38-5P, 1-(4-Methoxyphenylsulfonyl)-(2S)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-40-9P, 1-(4-Methoxyphenylsulfonyl)-(2S)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-42-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-methoxypyrrolidine 204071-43-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2-benzothiazolylthio)pyrrolidine 204071-44-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-(2-benzothiazolylthio)pyrrolidine 204071-45-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-methyl-2-imidazolylthio)pyrrolidine 204071-46-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-(1-methyl-2-imidazolylthio)pyrrolidine 204071-47-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-phenoxy-pyrrolidine 204071-48-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[4-(benzyloxy)phenoxy]pyrrolidine 204071-49-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-phenylaminophenoxy)pyrrolidine 204071-50-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-pyridinyloxy)pyrrolidine 204071-51-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-phenylthiopyrrolidine 204071-52-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(4-methoxyphenylthio)pyrrolidine 204071-53-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methoxyphenylthio)pyrrolidine 204071-54-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-ethoxymethoxypyrrolidine 204071-55-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-benzyloxymethoxypyrrolidine 204071-56-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-[(2-methoxyethoxy)methoxy]pyrrolidine 204071-57-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-mercaptopyrrolidine 204071-58-9P 204071-59-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-ethylpyrrolidine 204071-60-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-phenylpyrrolidine 204071-62-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-3,3-dimethyl-(4R)-hydroxypyrrolidine 204071-63-6P, 1-(4-Methylphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-64-7P, 1-(3,4-Dimethoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-65-8P, 1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-66-9P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-67-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-68-1P, 1-(4-Bromobenzenesulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-69-2P, 1-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-70-5P, 1-(2,4-Dichlorophenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-72-7P, 1-(4-Phenoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-73-8P,

1-(4-Isobutyloxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-74-9P, 1-(2-Methyl-4-bromophenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methoxyphenylthio)pyrrolidine 204071-75-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2-benzothiazolylthio)pyrrolidine 204071-76-1P, 1-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2-benzothiazolylthio)pyrrolidine 204071-77-2P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(4-methoxyphenylthio)pyrrolidine 204071-78-3P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-pyridyloxy)pyrrolidine 204071-79-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-aminopyrrolidine 204071-81-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-propylaminopyrrolidine 204071-82-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(hexylamino)pyrrolidine 204071-83-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2-phenylethylamino)pyrrolidine 204071-84-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(N-butyl-N-hexylamino)pyrrolidine 204071-86-3P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(methanesulfonyl)amino]pyrrolidine 204071-88-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(3-pyridylmethyl)-N-(methanesulfonyl)amino]pyrrolidine 204071-89-6P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[bis(methanesulfonyl)amino]pyrrolidine 204071-90-9P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(methanesulfonyl)-N-propylamino]pyrrolidine 204071-91-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(4-methoxyphenylsulfonyl)amino]pyrrolidine 204071-92-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(hexanoylamino)pyrrolidine 204071-94-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(methylcarbonyl)amino]pyrrolidine 204071-95-4P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(1-oxo-(2R)-benzyloxypropyl)amino]pyrrolidine 204071-96-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(1-oxo-(2R)-benzyloxy-3-phenylpropyl)amino]pyrrolidine 204071-98-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(1-oxo-(2R)-hydroxy-3-phenylpropyl)-N-propylamino]pyrrolidine 204071-99-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-00-4P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-01-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(morpholino)pyrrolidine 204072-02-6P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(morpholino)pyrrolidine 204072-03-7P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-04-8P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-05-9P 204072-06-0P 204072-07-1P 204072-08-2P 204072-09-3P 204072-10-6P 204072-11-7P 204072-14-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-4,4-bis(ethylthio)pyrrolidine 537704-26-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 537704-29-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[4-(1,1,3,3-tetramethylbutyl)phenoxy]pyrrolidine 537704-34-0P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[[1-methyl-3-imidazolyl)sulfonyl]amino]pyrrolidine 537704-36-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(4-biphenylamino)pyrrolidine 537704-43-1P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(1-oxo-(2R)-hydroxypropyl)-N-propylamino]pyrrolidine 722550-50-7P, 1-[4-(2-Methoxyethyl)phenylsulfonyl]-(2R)-(N-hydroxycarboxamido)-(4R)-

hydroxypyrrolidine 722550-51-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-hydroxycarboxamido-(4S)-[(methanesulfonyl)amino]pyrrolidine 722550-55-2P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-5-pyrrolidinone
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as **metalloprotease** inhibitors for treatment of restenosis)

IT 60-56-0, 2-Mercapto-1-methylimidazole 65-85-0, Benzoic acid, reactions 74-88-4, Methyl iodide, reactions 75-08-1, **Ethanethiol** 77-71-4, 5,5-Dimethylhydantoin 98-58-8, 4-Bromobenzenesulfonyl chloride 98-59-9, p-Toluenesulfonyl chloride 98-68-0, 4-Methoxyphenylsulfonyl chloride 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 100-58-3, Phenylmagnesium bromide 101-18-8, 3-Hydroxydiphenylamine 103-16-2, 4-(Benzyloxy)phenol 108-95-2, Phenol, reactions 108-98-5, **Thiophenol**, reactions 109-00-2, 3-Hydroxypyridine 111-26-2, Hexylamine 111-30-8, Glutaric dialdehyde 122-78-1, Phenylacetaldehyde 123-38-6, Propionaldehyde, reactions 124-63-0, Methanesulfonyl chloride 140-66-9, 4-Octylphenol 142-61-0, Hexanoyl chloride 149-30-4, 2-Mercaptobenzothiazole 358-23-6 500-22-1, 3-Pyridinecarboxaldehyde 507-09-5, **Thioacetic** acid, reactions 616-04-6, 1-Methylhydantoin 624-83-9, Methyl isocyanate 696-63-9, 4-Methoxythiophenol 925-90-6, Ethylmagnesium bromide 1138-56-3, p-Butoxyphenylsulfonyl chloride 1499-56-5, trans-4-Hydroxy-L-proline methyl ester 1623-92-3, 4-Phenoxyphenylsulfonyl chloride 2051-62-9, 4-Biphenyllyl chloride 2584-71-6, D-cis-4-Hydroxyproline 3188-13-4, Ethyl chloromethyl ether 3366-93-6, 1-Allylhydantoin 3587-60-8, Benzyl chloromethyl ether 3970-21-6, (2-Methoxyethoxy)methyl chloride 4042-36-8, (2R)-2-Carboxy-5-pyrrolidinone 5414-19-7, 2-Bromoethyl ether 6482-24-2, 2-Bromoethyl methyl ether 7617-67-6, Bis(2-bromoethyl) sulfone 15570-12-4, 3-Methoxythiophenol 16271-33-3, 2,4-Dichlorobenzenesulfonyl chloride 18092-54-1, 2-Nitro-4-methoxybenzenesulfonyl chloride 20312-36-1, L-3-Phenyllactic acid 23095-31-0, 3,4-Dimethoxyphenylsulfonyl chloride 33106-32-0, O-Benzyl-L-lactic acid 40856-73-3, (L)-5-Methylhydantoin 51212-37-4 81102-38-7, cis-4-Hydroxy-L-proline methyl ester 114676-47-0, cis-4-Hydroxy-D-proline methyl ester 139937-37-4, 2-Methyl-4-bromobenzenesulfonyl chloride 537704-27-1, Hydroxylamine monopotassium salt 537704-33-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as **metalloprotease** inhibitors for treatment of restenosis)

=> d ibib abs ed hitind hitstr retable l21 3-

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 26 ANSWERS - CONTINUE? Y/(N):y

L21 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:485162 HCAPLUS

DOCUMENT NUMBER: 141:38534

TITLE: Preparation of aromatic sulfone hydroxamic acid

metalloprotease inhibitors

INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Carroll, Jeffrey N.; Decrescenzo, Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman, Daniel P.; McDonald, Joseph J.; Li, Madeleine H.;

PATENT ASSIGNEE(S):

SOURCE:

DOCUMENT TYPE:

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

Hockerman, Susan L.; Howard, Susan C.; Kolodziej,
 Steve A.; Mischke, Deborah A.; Rico, Joseph G.;
 Stehle, Nathan W.; Tollefson, Michael B.; Vernier,
 William F.; Villamil, Clara I.
 Pharmacia Corporation, USA
 U.S., 403 pp., Cont.-in-part of U.S. Ser. No. 311,837.
 CODEN: USXXAM

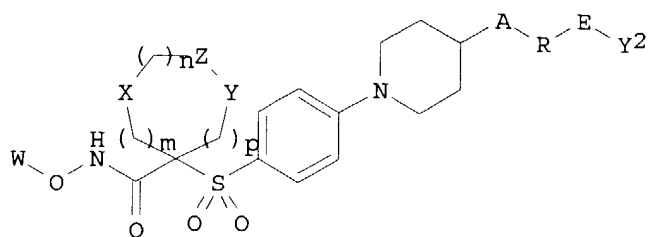
Patent
 English

5

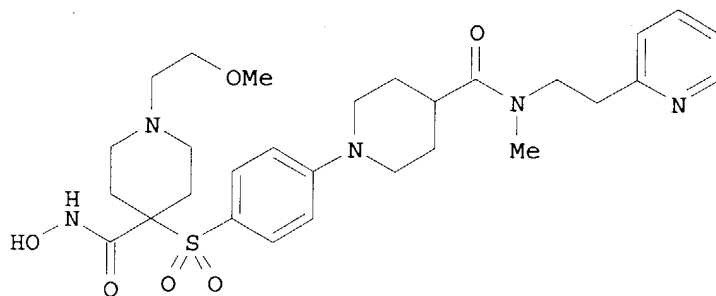
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6750228	B1	20040615	US 2000-570731	20000512
US 2001014688	A1	20010816	US 1998-191129	19981113
US 2001039287	A1	20011108	US 1999-256948	19990224
CA 2372934	AA	20001123	CA 2000-2372934	20000515
WO 2000069821	A1	20001123	WO 2000-US6719	20000515
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1183239	A1	20020306	EP 2000-930088	20000515
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
BR 2000010562	A	20030610	BR 2000-10562	20000515
JP 2003520196	T2	20030702	JP 2000-618238	20000515
AU 766792	B2	20031023	AU 2000-47970	20000515
NZ 515217	A	20040430	NZ 2000-515217	20000515
US 2002177588	A1	20021128	US 2001-954451	20010917
US 6750233	B2	20040615		
ZA 2001009006	A	20021202	ZA 2001-9006	20011031
NO 2001005543	A	20020110	NO 2001-5543	20011113
US 2003073718	A1	20030417	US 2001-989943	20011121
US 6683093	B2	20040127		
US 2004209914	A1	20041021	US 2003-730403	20031208
US 2004235818	A1	20041125	US 2003-747796	20031229
PRIORITY APPLN. INFO.:			US 1997-66007P	P 19971114
			US 1998-95347P	P 19980804
			US 1998-101080P	P 19980918
			US 1999-256948	B2 19990224
			US 1999-311837	A2 19990514
			US 1998-95501P	P 19980806
			US 1998-186410	B2 19981105
			US 1998-191129	B2 19981113
			US 2000-570731	A 20000512
			WO 2000-US6719	W 20000515
			US 2001-989943	A3 20011121

OTHER SOURCE(S):
 GI

MARPAT 141:38534



I



II

AB A treatment process is disclosed that comprises administering an effective amount of an aromatic sulfone hydroxamic acid I [W = H, cation, certain acyl or thioacyl groups; m, n, p = 0-2; (m+n+p) = 1 to 4; Z = (un)substituted NH; X, Y = (un)substituted CH₂; A = bond, O, S, (un)substituted NH, COO, OCO, CH:CH, C.tplbond.C, N:N, NHNH, NHCOO, (un)substituted CONH, NHCO, etc.; R = alkylene, arylene, heteroarylene, etc., with provisos; E = bond, CONH, NHCO, CO, SO₂, NHSO₂, SO₂NH, S, etc.; Y₂ = absent, H, alkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.] to a host having a condition associated with pathol. matrix **metalloprotease** (**MMP**) activity. I exhibit excellent inhibitory activity of one or more **MMP** enzymes, such as **MMP**-2, **MMP**-9 and **MMP**-13, while exhibiting substantially less inhibition of (at least) **MMP**-1 (biol. data given). Also disclosed are **metalloprotease** inhibitor compds. having such selective activities, processes for manufacture of such compds., and pharmaceutical compns. using such inhibitors. The compds. are potentially useful against a wide variety of conditions, notably as antiosteoarthritic, antiangiogenesis, and antitumor agents. Over 900 example compds. are listed, most with supporting phys. data, and many with synthetic details. E.g., a multi-step synthesis of the compound II.2HCl was given.

ED Entered STN: 16 Jun 2004

IC ICM A61K031-445

ICS C07D211-06

NCL 514316000; 514318000; 514328000; 514330000; 546189000; 546193000; 546220000; 546225000

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 7, 63

ST arom sulfone hydroxamic acid prepn matrix **metalloprotease** inhibitor; **MMP** inhibitor prepn hydroxamic acid pyran **thiopyran** piperidine; osteoarthritis arom sulfone hydroxamic acid prepn; antitumor arom sulfone hydroxamic acid prepn; angiogenesis arom sulfone hydroxamic acid prepn

IT Angiogenesis

Angiogenesis inhibitors

Anti-inflammatory agents

Antiarthritics
 Antitumor agents
 Drug delivery systems
 Human
 Neoplasm
 Osteoarthritis
 (preparation of aromatic sulfone hydroxamic acids as **metalloprotease**
 inhibitors)

IT Hydroxamic acids

Sulfones

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of aromatic sulfone hydroxamic acids as **metalloprotease**
 inhibitors)

IT 9001-12-1, **MMP-1** 141907-41-7, Matrix **metalloprotease**
 146480-35-5, **MMP 2** 146480-36-6, **MMP 9** 175449-82-8,
MMP-13

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (binding; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT 308822-81-3P 308822-82-4P 308822-86-8P 308822-95-9P 308823-05-4P
 308824-05-7P 308824-24-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT 226390-98-3P 226391-00-0P 226391-03-3P 226391-36-2P 226391-57-7P
 226391-61-3P 226392-57-0P 226392-69-4P 226393-71-1P 226393-73-3P
 226393-97-1P 226393-99-3P 226396-25-4P 226396-28-7P 289486-35-7P
 289486-36-8P 308821-65-0P 308821-66-1P 308821-67-2P 308821-69-4P
 308821-71-8P 308821-72-9P 308821-73-0P 308821-74-1P 308821-75-2P
 308821-76-3P 308821-77-4P 308821-79-6P 308821-81-0P 308821-82-1P
 308821-83-2P 308821-85-4P 308821-87-6P 308821-89-8P 308821-91-2P
 308821-93-4P 308821-95-6P 308821-96-7P 308821-97-8P 308821-98-9P
 308821-99-0P 308822-00-6P 308822-01-7P 308822-02-8P 308822-03-9P
 308822-04-0P 308822-05-1P 308822-06-2P 308822-07-3P 308822-08-4P
 308822-09-5P 308822-11-9P 308822-13-1P 308822-14-2P 308822-16-4P
 308822-17-5P 308822-18-6P 308822-19-7P 308822-21-1P 308822-22-2P
 308822-23-3P 308822-24-4P 308822-26-6P 308822-28-8P 308822-29-9P
 308822-30-2P 308822-31-3P 308822-32-4P 308822-33-5P 308822-34-6P
 308822-35-7P 308822-36-8P 308822-38-0P 308822-41-5P 308822-42-6P
 308822-44-8P 308822-45-9P 308822-46-0P 308822-49-3P 308822-51-7P
 308822-53-9P 308822-54-0P 308822-56-2P 308822-58-4P 308822-60-8P
 308822-63-1P 308822-64-2P 308822-66-4P 308822-69-7P 308822-71-1P
 308822-72-2P 308822-73-3P 308822-74-4P 308822-75-5P 308822-77-7P
 308822-78-8P 308822-79-9P 308822-80-2P 308822-83-5P 308822-84-6P
 308822-85-7P 308822-87-9P 308822-88-0P 308822-89-1P 308822-90-4P
 308822-91-5P 308822-92-6P 308822-93-7P 308822-94-8P 308822-96-0P
 308822-97-1P 308822-98-2P 308822-99-3P 308823-00-9P 308823-01-0P
 308823-02-1P 308823-03-2P 308823-04-3P 308823-06-5P 308823-07-6P
 308823-08-7P 308823-09-8P 308823-10-1P 308823-11-2P 308823-12-3P
 308823-13-4P 308823-14-5P 308823-15-6P 308823-16-7P 308823-17-8P
 308823-18-9P 308823-19-0P 308823-20-3P 308823-21-4P 308823-22-5P
 308823-23-6P 308823-24-7P 308823-25-8P 308823-26-9P 308823-27-0P
 308823-28-1P 308823-29-2P 308823-30-5P 308823-31-6P 308823-32-7P
 308823-33-8P 308823-34-9P 308823-35-0P 308823-36-1P 308823-37-2P
 308823-38-3P 308823-39-4P 308823-40-7P 308823-41-8P 308823-42-9P
 308823-43-0P 308823-44-1P 308823-45-2P 308823-46-3P 308823-47-4P

308823-48-5P	308823-49-6P	308823-50-9P	308823-51-0P	308823-52-1P
308823-53-2P	308823-54-3P	308823-55-4P	308823-56-5P	308823-57-6P
308823-58-7P	308823-59-8P	308823-60-1P	308823-61-2P	308823-62-3P
308823-63-4P	308823-64-5P	308823-65-6P	308823-66-7P	308823-67-8P
308823-68-9P	308823-69-0P	308823-70-3P	308823-71-4P	308823-72-5P
308823-73-6P	308823-74-7P	308823-75-8P	308823-76-9P	308823-77-0P
308823-78-1P	308823-79-2P	308823-80-5P	308823-81-6P	308823-82-7P
308823-83-8P	308823-84-9P	308823-85-0P	308823-86-1P	308823-87-2P
308823-91-8P	308823-92-9P	308823-93-0P	308823-94-1P	308823-95-2P
308823-96-3P	308823-97-4P	308823-98-5P	308823-99-6P	308824-00-2P
308824-01-3P	308824-02-4P	308824-03-5P	308824-04-6P	308824-06-8P
308824-07-9P	308824-08-0P	308824-09-1P	308824-10-4P	308824-11-5P
308824-12-6P	308824-13-7P	308824-14-8P	308824-15-9P	308824-16-0P
308824-17-1P	308824-18-2P	308824-19-3P	308824-20-6P	308824-21-7P
308824-22-8P	308824-23-9P	308824-25-1P	308824-26-2P	308824-27-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)

IT	308824-28-4P	308824-29-5P	308824-30-8P	308824-31-9P	308824-32-0P
	308824-33-1P	308824-34-2P	308824-35-3P	308824-36-4P	308824-37-5P
	308824-38-6P	308824-39-7P	308824-40-0P	308824-41-1P	308824-42-2P
	308824-43-3P	308824-44-4P	308824-45-5P	308824-46-6P	308824-47-7P
	308824-48-8P	308824-49-9P	308824-50-2P	308824-51-3P	308824-52-4P
	308824-53-5P	308824-54-6P	308824-55-7P	308824-56-8P	308824-57-9P
	308824-58-0P	308824-59-1P	308824-60-4P	308824-61-5P	308824-62-6P
	308824-63-7P	308824-64-8P	308824-65-9P	308824-66-0P	308824-69-3P
	308824-71-7P	308824-73-9P	308824-75-1P	308824-77-3P	308824-79-5P
	308824-81-9P	308824-83-1P	308824-85-3P	308824-86-4P	308824-87-5P
	308824-88-6P	308824-89-7P	308824-90-0P	308824-91-1P	308824-92-2P
	308824-93-3P	308824-94-4P	308824-95-5P	308824-96-6P	308824-97-7P
	308824-98-8P	308824-99-9P	308825-00-5P	308825-01-6P	308825-02-7P
	308825-03-8P	308825-04-9P	308825-05-0P	308825-06-1P	308825-07-2P
	308825-08-3P	308825-09-4P	308825-10-7P	308825-11-8P	308825-12-9P
	308825-13-0P	308825-14-1P	308825-15-2P	308825-16-3P	308825-17-4P
	308825-18-5P	308825-19-6P	308825-20-9P	308825-21-0P	308825-22-1P
	308825-23-2P	308825-24-3P	308825-25-4P	308825-26-5P	308825-27-6P
	308825-28-7P	308825-29-8P	308825-30-1P	308825-31-2P	308825-32-3P
	308825-33-4P	308825-34-5P	308825-35-6P	308825-36-7P	308825-37-8P
	308825-38-9P	308825-39-0P	308825-40-3P	308825-41-4P	308825-42-5P
	308825-43-6P	308825-44-7P	308825-45-8P	308825-46-9P	308825-47-0P
	308825-48-1P	308825-49-2P	308825-50-5P	308825-51-6P	308825-52-7P
	308825-53-8P	308825-54-9P	308825-55-0P	308825-56-1P	308825-57-2P
	308825-58-3P	308825-59-4P	308825-60-7P	308825-61-8P	308825-62-9P
	308825-63-0P	308825-64-1P	308825-65-2P	308825-66-3P	308825-67-4P
	308825-68-5P	308825-69-6P	308825-70-9P	308825-71-0P	308825-72-1P
	308825-73-2P	308825-74-3P	308825-76-5P	308825-78-7P	308825-79-8P
	308825-80-1P	308825-81-2P	308825-83-4P	308825-85-6P	308825-86-7P
	308825-87-8P	308825-88-9P	308825-89-0P	308825-90-3P	308825-92-5P
	308825-93-6P	308825-94-7P	308825-95-8P	308825-96-9P	308825-97-0P
	308825-98-1P	308825-99-2P	308826-00-8P	308826-01-9P	308826-02-0P
	308826-04-2P	308826-05-3P	308826-06-4P	308826-07-5P	308826-08-6P
	308826-09-7P	308826-10-0P	308826-11-1P	308826-12-2P	308826-13-3P
	308826-14-4P	308826-15-5P	308826-16-6P	308826-17-7P	308826-18-8P
	308826-19-9P	308826-20-2P	308826-21-3P	308826-23-5P	308826-25-7P
	308826-26-8P	308826-27-9P	308826-28-0P	308826-29-1P	308826-30-4P
	308826-31-5P	308826-32-6P	308826-34-8P	308826-36-0P	308826-37-1P
	308826-39-3P	308826-41-7P	308826-43-9P	308826-44-0P	308826-45-1P
	308826-46-2P	308826-47-3P	308826-48-4P	308826-49-5P	308826-50-8P

308826-51-9P	308826-52-0P	308826-53-1P	308826-54-2P	308826-55-3P
308826-57-5P	308826-58-6P	308826-59-7P	308826-60-0P	308826-61-1P
308826-62-2P	308826-63-3P	308826-64-4P	308826-65-5P	308826-66-6P
308826-67-7P	308826-69-9P	308826-70-2P	308826-71-3P	308826-72-4P
308826-73-5P	308826-74-6P	308826-75-7P	308826-76-8P	308826-77-9P
308826-78-0P	308826-80-4P	308826-82-6P	308826-83-7P	308826-84-8P
308826-85-9P	308826-86-0P	308826-88-2P	308826-90-6P	308826-92-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT	308826-93-9P	308826-94-0P	308826-95-1P	308826-96-2P	308826-97-3P
	308826-98-4P	308826-99-5P	308827-00-1P	308827-01-2P	308827-02-3P
	308827-03-4P	308827-04-5P	308827-05-6P	308827-06-7P	308827-07-8P
	308827-08-9P	308827-09-0P	308827-10-3P	308827-11-4P	308827-12-5P
	308827-13-6P	308827-14-7P	308827-15-8P	308827-16-9P	308827-17-0P
	308827-18-1P	308827-19-2P	308827-20-5P	308827-21-6P	308827-22-7P
	308827-23-8P	308827-24-9P	308827-25-0P	308827-26-1P	308827-27-2P
	308827-28-3P	308827-29-4P	308827-30-7P	308827-32-9P	308827-33-0P
	308827-34-1P	308827-35-2P	308827-36-3P	308827-37-4P	308827-38-5P
	308827-39-6P	308827-40-9P	308827-41-0P	308827-42-1P	308827-43-2P
	308827-44-3P	308827-45-4P	308827-46-5P	308827-47-6P	308827-48-7P
	308827-49-8P	308827-50-1P	308827-51-2P	308827-52-3P	308827-53-4P
	308827-54-5P	308827-55-6P	308827-56-7P	308827-57-8P	308827-58-9P
	308827-59-0P	308827-60-3P	308827-61-4P	308827-62-5P	308827-63-6P
	308827-64-7P	308827-65-8P	308827-66-9P	308827-67-0P	308827-68-1P
	308827-69-2P	308827-70-5P	308827-72-7P	308827-74-9P	308827-75-0P
	308827-77-2P	308827-78-3P	308827-79-4P	308827-80-7P	308827-81-8P
	308827-82-9P	308827-83-0P	308827-84-1P	308827-85-2P	308827-86-3P
	308827-87-4P	308827-88-5P	308827-89-6P	308827-90-9P	308827-91-0P
	308827-92-1P	308827-93-2P	308827-94-3P	308827-95-4P	308827-96-5P
	308827-97-6P	308827-98-7P	308827-99-8P	308828-00-4P	308828-01-5P
	308828-02-6P	308828-03-7P	308828-04-8P	308828-05-9P	308828-06-0P
	308828-07-1P	308828-08-2P	308828-09-3P	308828-10-6P	308828-11-7P
	308828-12-8P	308828-13-9P	308828-14-0P	308828-15-1P	308828-16-2P
	308828-17-3P	308828-18-4P	308828-19-5P	308828-20-8P	308828-21-9P
	308828-22-0P	308828-23-1P	308828-24-2P	308828-25-3P	308828-26-4P
	308828-27-5P	308828-28-6P	308828-29-7P	308828-30-0P	308828-31-1P
	308828-33-3P	308828-34-4P	308828-35-5P	308828-36-6P	308828-37-7P
	308828-39-9P	308828-40-2P	308828-41-3P	308828-42-4P	308828-43-5P
	308828-44-6P	308828-45-7P	308828-46-8P	308828-47-9P	308828-48-0P
	308828-49-1P	308828-50-4P	308828-51-5P	308828-52-6P	308828-53-7P
	308828-54-8P	308828-55-9P	308828-56-0P	308828-57-1P	308828-58-2P
	308828-59-3P	308828-60-6P	308828-61-7P	308828-62-8P	308828-63-9P
	308828-64-0P	308828-65-1P	308828-66-2P	308828-68-4P	308828-69-5P
	308828-70-8P	308828-71-9P	308828-72-0P	308828-73-1P	308828-74-2P
	308828-75-3P	308828-76-4P	308828-77-5P	308828-78-6P	308828-79-7P
	308828-80-0P	308828-81-1P	308828-82-2P	308828-83-3P	308828-84-4P
	308828-85-5P	308828-86-6P	308828-87-7P	308828-88-8P	308828-89-9P
	308828-90-2P	308828-91-3P	308828-92-4P	308828-93-5P	308828-94-6P
	308828-95-7P	308828-96-8P	308828-97-9P	308828-98-0P	308828-99-1P
	308829-00-7P	308829-01-8P	308829-02-9P	308829-03-0P	308829-04-1P
	308829-05-2P	308829-06-3P	308829-07-4P	308829-08-5P	308829-09-6P
	308829-10-9P	308829-11-0P	308829-12-1P	308829-13-2P	308829-14-3P
	308829-15-4P	308829-16-5P	308829-17-6P	308829-19-8P	308829-20-1P
	308829-21-2P	308829-23-4P	308829-24-5P	308829-25-6P	308829-26-7P
	308829-27-8P	308829-28-9P	308829-29-0P	308829-32-5P	308829-34-7P
	308829-35-8P	308829-36-9P	308829-37-0P	308829-38-1P	308829-39-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT	308829-40-5P	308829-41-6P	308829-42-7P	308829-43-8P	308829-44-9P
	308829-45-0P	308829-46-1P	308829-47-2P	308829-48-3P	308829-49-4P
	308829-51-8P	308829-53-0P	308829-54-1P	308829-55-2P	308829-56-3P
	308829-57-4P	308829-58-5P	308829-59-6P	308829-60-9P	308829-61-0P
	308829-62-1P	308829-63-2P	308829-64-3P	308829-65-4P	308829-66-5P
	308829-67-6P	308829-68-7P	308829-69-8P	308829-70-1P	308829-71-2P
	308829-72-3P	308829-73-4P	308829-74-5P	308829-75-6P	308829-76-7P
	308832-77-1P	308832-78-2P			

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT	405-31-2P	4783-86-2P	81151-35-1P	84358-13-4P	113113-66-9P
	138647-49-1P	142851-03-4P	162881-76-7P	180695-79-8P	188527-08-4P
	192329-80-9P	192330-49-7P	193022-95-6P	195503-42-5P	226388-52-9P
	226388-56-3P	226388-60-9P	226389-21-5P	226389-49-7DP, resin-bound	
	226389-52-2P	226391-07-7DP, resin-bound	226395-65-9P	226395-75-1P	
	226395-93-3P	226396-02-7P	226396-03-8P	226396-33-4P	226396-34-5P
	226396-40-3P	226396-42-5P	226396-44-7P	226396-51-6P	226396-53-8P
	226396-54-9P	226396-56-1P	226396-62-9P	226396-63-0P	226396-64-1P
	226396-65-2P	226396-66-3P	226396-67-4P	226396-70-9P	226396-71-0P
	226396-72-1P	226397-96-2P	226398-02-3P	226398-13-6P	226399-44-6P
	226399-45-7P	226399-47-9P	226399-49-1P	226399-50-4P	226399-52-6P
	226399-90-2P	226399-91-3P	226399-92-4P	226399-95-7P	226400-29-9P
	226400-78-8P	226400-79-9P	226400-80-2P	226401-17-8P	226401-18-9P
	226401-19-0P	226401-21-4P	226401-22-5P	226401-23-6P	226401-67-8P
	226401-76-9P	287954-32-9P	308798-39-2P	308823-36-1DP, resin-bound	
	308823-46-3DP, resin-bound		308823-88-3P	308823-89-4P	308823-90-7P
	308829-77-8DP, resin-bound		308829-78-9P	308829-79-0DP, resin-bound	
	308829-80-3DP, resin-bound		308829-81-4DP, resin-bound	308829-82-5P	
	308829-83-6P	308829-84-7P	308829-85-8P	308829-87-0P	308829-88-1P
	308829-89-2P	308829-90-5P	308829-91-6P	308829-92-7P	308829-93-8P
	308829-94-9P	308829-95-0P	308829-96-1P	308829-97-2P	308829-98-3P
	308829-99-4P	308830-00-4P	308830-01-5P	308830-02-6P	308830-03-7P
	308830-04-8P	308830-05-9P	308830-07-1P	308830-09-3P	308830-11-7P
	308830-13-9P	308830-15-1P	308830-17-3P	308830-19-5P	308830-20-8P
	308830-22-0P	308830-24-2P	308830-26-4P	308830-29-7P	308830-30-0P
	308830-32-2P	308830-34-4P	308830-36-6P	308830-38-8P	308830-39-9P
	308830-41-3P	308830-43-5P	308830-45-7P	308830-47-9P	308830-49-1P
	308830-50-4P	308830-51-5P	308830-52-6P	308830-53-7P	308830-54-8P
	308830-55-9P	308830-56-0P	308830-57-1P	308830-58-2P	308830-59-3P
	308830-60-6P	308830-61-7P	308830-62-8P	308830-63-9P	308830-64-0P
	308830-65-1P	308830-66-2P	308830-67-3P	308830-68-4P	308830-69-5P
	308830-70-8P	308830-71-9P	308830-72-0P	308830-73-1P	308830-74-2P
	308830-75-3P	308830-76-4P	308830-77-5P	308830-78-6P	308830-79-7P
	308830-80-0P	308830-81-1P	308830-82-2P	308830-83-3P	308830-84-4P
	308830-85-5P	308830-86-6P	308830-87-7P	308830-88-8P	308830-89-9P
	308830-90-2P	308830-91-3P	308830-92-4P	308830-93-5P	308830-94-6P
	308830-95-7P	308830-96-8P	308830-97-9P		

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(intermediate; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT	51-45-6, Histamine, reactions	62-53-3, Aniline, reactions	67-62-9, Methoxyamine	75-04-7, Ethylamine, reactions	78-81-9, Isobutylamine
----	-------------------------------	-----------------------------	-----------------------	--------------------------------	------------------------

90-04-0 95-51-2, 2-Chloroaniline 96-34-4, Methyl 2-chloroacetate
 98-09-9, Benzenesulfonyl chloride 98-16-8, 3-(Trifluoromethyl)aniline
 98-88-4, Benzoyl chloride 99-89-8, 4-Isopropylphenol 99-98-9,
 N,N-Dimethyl-p-phenylenediamine 100-07-2, 4-Anisoyl chloride 100-39-0,
 Benzyl bromide 100-46-9, Benzylamine, reactions 100-61-8,
 N-Methylaniline, reactions 103-67-3, N-Benzylmethylamine 103-71-9,
 Phenyl isocyanate, reactions 103-76-4, N-(2-Hydroxyethyl)piperazine
 103-80-0, Phenylacetyl chloride 104-12-1, 4-Chlorophenyl isocyanate
 104-81-4, 4-Methylbenzyl bromide 104-94-9 106-38-7, 4-Bromotoluene
 106-96-7, Propargyl bromide 107-08-4, 1-Iodopropane 107-10-8,
 1-Propylamine, reactions 108-00-9, N,N-Dimethylethylenediamine
 108-42-9, 3-Chloroaniline 108-95-2, Phenol, reactions 108-98-5,
Thiophenol, reactions 109-00-2, 3-Hydroxypyridine 109-01-3,
 1-Methylpiperazine 109-85-3, 2-Methoxyethylamine 109-89-7,
 Diethylamine, reactions 109-90-0, Ethyl isocyanate 110-85-0,
 Piperazine, reactions 110-89-4, Piperidine, reactions 110-91-8,
 Morpholine, reactions 110-96-3, Diisobutylamine 111-49-9 111-95-5
 122-04-3, 4-Nitrobenzoyl chloride 122-99-6, Ethylene glycol phenyl ether
 123-75-1, Pyrrolidine, reactions 123-90-0, **Thiomorpholine**
 124-02-7 124-40-3, Dimethylamine, reactions 141-43-5, Ethanolamine,
 reactions 142-25-6, N,N,N'-Trimethylethylenediamine 150-76-5,
 4-Methoxyphenol 156-87-6, 3-Amino-1-propanol 288-32-4, Imidazole,
 reactions 288-88-0, 1H-1,2,4-Triazole 312-94-7, 2-
 (Trifluoromethyl)benzoyl chloride 329-01-1, 3-(Trifluoromethyl)phenyl
 isocyanate 329-15-7, 4-(Trifluoromethyl)benzoyl chloride 348-54-9,
 2-Fluoroaniline 371-40-4, 4-Fluoroaniline 371-41-5, 4-Fluorophenol
 371-42-6, 4-(Fluoro)**thiophenol** 372-19-0, 3-Fluoroaniline
 393-52-2, 2-Fluorobenzoyl chloride 395-44-8, 2-(Trifluoromethyl)benzyl
 bromide 402-23-3, 3-(Trifluoromethyl)benzyl bromide 402-45-9,
 α,α,α -Trifluoro-p-cresol 403-43-0, 4-Fluorobenzoyl
 chloride 404-71-7, 3-Fluorophenyl isocyanate 407-25-0, Trifluoroacetic
 anhydride 421-83-0, Trifluoromethanesulfonyl chloride 455-14-1,
 4-(Trifluoromethyl)aniline 459-46-1, 4-Fluorobenzyl bromide 461-82-5,
 4-(Trifluoromethoxy)aniline 461-84-7, 4-(**Trifluoromethylthio**
)phenol 496-15-1, Indoline 498-94-2, Isonipecotic acid 504-24-5,
 4-Aminopyridine 527-69-5, 2-Furoyl chloride 536-90-3 556-61-6,
 Methyl **isothiocyanate** 591-54-8, 4-Aminopyrimidine 592-55-2,
 2-Bromoethyl ethyl ether 616-45-5, 2-Pyrrolidinone 620-13-3,
 3-Methylbenzyl bromide 622-95-7, 4-Chlorobenzyl bromide 625-43-4,
 N-Methylisobutylamine 626-56-2, 3-Methylpiperidine 626-64-2,
 4-Hydroxypyridine 627-37-2, N-Methylallylamine 658-46-8 694-05-3,
 1,2,3,6-Tetrahydropyridine 753-90-2, 2,2,2-Trifluoroethylamine
 777-44-6, 3-(Trifluoromethyl)benzenesulfonyl chloride 828-27-3,
 p-(Trifluoromethoxy)phenol 874-60-2, 4-Toluoyl chloride 877-88-3,
 3,5-Dimethoxybenzyl bromide 877-96-3, 1-[3-(Dimethylamino)propyl]piperaz
 ine 929-06-6, 2-(2-Aminoethoxy)ethanol 933-88-0, 2-Toluoyl chloride
 1008-91-9, 1-(4-Pyridyl)piperazine 1011-15-0, 1-(2-
 Fluorophenyl)piperazine 1013-76-9, 1-(2,4-Dimethylphenyl)piperazine
 1126-09-6, Ethyl isonipecotate 1195-45-5, 4-Fluorophenyl isocyanate
 1423-27-4 1535-73-5, 3-(Trifluoromethoxy)aniline 1535-75-7,
 2-(Trifluoromethoxy)aniline 1548-13-6, 4-(Trifluoromethyl)phenyl
 isocyanate 1632-84-4, 4-(**Methylthio**)phenyl isocyanate
 1645-65-4, 4-(Trifluoromethyl)phenyl **isothiocyanate** 1711-05-3,
 3-Anisoyl chloride 1711-07-5, 3-Fluorobenzoyl chloride 1939-99-7,
 α -Toluenesulfonyl chloride 2033-89-8, 3,4-Dimethoxyphenol
 2038-57-5, Benzenepropanamine 2131-64-8, 4-(Dimethylamino)phenyl
isothiocyanate 2251-50-5, Pentafluorobenzoyl chloride
 2251-65-2, 3-(Trifluoromethyl)benzoyl chloride 2252-63-3,
 1-(4-Fluorophenyl)piperazine 2338-18-3 2516-47-4,
 (Aminomethyl)cyclopropane 2836-04-6, N,N-Dimethyl-1,3-phenylenediamine

2971-79-1, Methyl isonipecotate 2991-42-6, 4-(Trifluoromethyl)benzenesulfonyl chloride 3173-56-6, Benzyl isocyanate 3202-33-3, 4-Phenoxypiperidine 3282-30-2, Pivaloyl chloride 3535-37-3, 3,4-Dimethoxybenzoyl chloride 3644-18-6, 1-[2-(Dimethylamino)ethyl]piperazine 3647-69-6, 4-(2-Chloroethyl)morpholine hydrochloride 3731-51-9, 2-(Aminomethyl)pyridine 3731-52-0, 3-(Aminomethyl)pyridine 3731-53-1, 4-(Aminomethyl)pyridine 4023-34-1, Cyclopropanecarbonyl chloride 4124-31-6, Trichloroacetic anhydride 4318-37-0, 1-Methylhomopiperazine 4318-42-7 4597-87-9, 2-(Methylamino)pyridine 4693-91-8, 4-Methoxyphenylacetyl chloride 4755-50-4, 4-(Dimethylamino)benzoyl chloride 4892-89-1, 1-(2-Morpholinoethyl)piperazine 5181-06-6, 1-(2-Methoxyphenyl)piperidine 5271-67-0, 2-**Thiophenecarbonyl** chloride 5292-43-3, tert-Butyl bromoacetate 5321-49-3, 1-(2-Phenylethyl)piperazine 5382-16-1, 4-Hydroxypiperidine 5414-19-7, Bis-(2-bromoethyl) ether 5638-76-6, 2-[2-(Methylamino)ethyl]pyridine 6269-89-2, 1-(4-Nitrophenyl)piperazine 6457-49-4, 4-(Hydroxymethyl)piperidine 6482-24-2, 2-Bromoethyl methyl ether 6485-55-8, cis-2,6-Dimethylmorpholine 6640-24-0, 1-(3-Chlorophenyl)piperazine 6711-48-4, 3,3'-Iminobis(N,N-dimethylpropylamine) 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)hydroxylamine 7357-67-7, 3-Morpholinopropyl chloride 7377-26-6, Methyl 4-(chlorocarbonyl)benzoate 7379-35-3, 4-Chloropyridine hydrochloride 10111-08-7, 2-Imidazolecarboxaldehyde 10400-19-8, Nicotinoyl chloride 13339-01-0, 1-(2-Ethoxyphenyl)piperazine 13349-82-1, 1-[2-(2-Hydroxyethoxy)ethyl]piperazine 13484-40-7, 1-(2-Methoxyethyl)piperazine 13889-98-0, 1-Acetylpiperazine 13961-36-9, 1-Allylpiperazine 14254-57-0, Isonicotinoyl chloride 14446-75-4, cis-3,5-Dimethylpiperidine 15268-31-2, 3-Pyridyl isocyanate 16413-26-6, 3-Cyanophenyl isocyanate 16744-98-2, 2-Fluorophenyl isocyanate 17201-43-3, 4-Cyanobenzyl bromide 17213-57-9, 3,5-Dimethoxybenzoyl chloride 17452-27-6 17739-45-6, 2-(2-Bromoethoxy)tetrahydro-2H-pyran 18880-04-1, 3,4-Dichlorobenzyl bromide 19853-09-9, 2-Phenylbenzyl bromide 20662-53-7 20980-22-7, 2-(1-Piperazinyl)pyrimidine 21043-40-3, 1-Cyclopentylpiperazine 21615-34-9, 2-Anisoyl chloride 21655-48-1, cis-2,6-Dimethylpiperazine 26389-60-6, N-Propylcyclopropanemethylamine 27129-86-8, 3,5-Dimethylbenzyl bromide 27374-25-0, [(1-Ethoxycyclopropyl)oxy]trimethylsilane 27757-85-3, 2-**Thiophenemethylamine** 30459-17-7, 1-[4-(Trifluoromethyl)phenyl]piperazine 32452-46-3, trans-3,5-Dimethylpiperidine 32459-62-4, 4-Ethoxyphenyl isocyanate 32813-24-4, 2-Piperidinoethyl **isothiocyanate** 33403-97-3, 4-(Ethylaminomethyl)pyridine 34803-66-2, 1-(2-Pyridyl)piperazine 34803-68-4, 1-(2-Pyrazinyl)piperazine 35161-71-8, N-Methylpropargylamine 35309-20-7, 3-Isocyanatopropionic acid 35386-24-4, 1-(2-Methoxyphenyl)piperazine 35730-09-7, 2,5-Difluorobenzoyl chloride 35794-11-7, 3,5-Dimethylpiperidine 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine 36823-88-8, 4-(Trifluoromethoxy)benzoyl chloride 37517-81-0, Methyl malonyl chloride 38778-05-1, 4-(Phenoxy)**benzenethiol** 39512-50-0, 1-(2-Chlorophenyl)piperazine 39546-32-2, Isonipecotamide 39890-45-4, N-[2-(1-Piperazinyl)acetyl]pyrrolidine 40004-08-8, 1-(Ethoxycarbonylmethyl)piperazine 40172-95-0, 1-(2-Furoyl)piperazine 45597-00-0, cis-3,5-Dimethylmorpholine 49647-20-3, 4-Acetylphenyl isocyanate 50824-05-0, 4-(Trifluoromethoxy)benzyl bromide 51639-48-6 53460-46-1, 1,3,3-Trimethyl-6-azabicyclo[3.2.1]octane 54288-70-9, 4-Bromopiperidine hydrobromide 56346-57-7, 4-(4-Fluorobenzoyl)piperidine 56651-60-6, 4-Methoxybenzyl isocyanate 58315-38-1, N-[2-Nitro-4-(trifluoromethyl)phenyl]piperazine 58333-75-8, 4-(2-Methoxyphenyl)piperidine 63224-35-1, 2-Morpholinoethyl **isothiocyanate** 68337-15-5, 4-(1,2,4-Triazol-1-yl)phenol

68832-13-3 69628-75-7, 1-(1-Phenylethyl)piperazine 76362-12-4,
 4-(4-Methoxybenzoyl)piperidine 76835-20-6, 1-(5-Chloro-2-
 methylphenyl)piperazine 79099-07-3 82911-69-1, N-(9-
 Fluorenylmethoxycarbonyloxy)succinimide 85118-01-0, 3,4-Difluorobenzyl
 bromide 85275-45-2 87394-63-6, 1-[3-(Trifluoromethyl)pyrid-2-
 yl]piperazine 103008-51-1, 2-(Trifluoromethoxy)benzenesulfonyl chloride
 109384-19-2 115761-79-0, 1-(2,4-Difluorophenyl)piperazine 118708-88-6,
 1-[4-(Trifluoromethyl)-2-pyridyl]piperazine 120104-92-9 132834-59-4,
 1-[3-Chloro-5-(trifluoromethyl)pyrid-2-yl]piperazine 159689-88-0,
 3-(Trifluoromethoxy)benzyl bromide 175277-80-2 179756-91-3,
 1-[4-(Trifluoromethyl)-2-pyrimidyl]piperazine 226400-27-7 308830-98-0
 RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT 308830-99-1 308831-00-7, 4-(3,5-Dimethylphenoxy)piperidine 308831-01-8
 RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
=====	=====	=====	=====	=====	=====
Anon	1988			EP 0266182	HCAPLUS
Anon	1990			WO 9005719	HCAPLUS
Anon	1992			JP 04-338331	HCAPLUS
Anon	1993			WO 9320047	HCAPLUS
Anon	1994			EP 0606046	HCAPLUS
Anon	1994			WO 9402466	HCAPLUS
Anon	1994			WO 9424140	HCAPLUS
Anon	1995			WO 9509841	HCAPLUS
Anon	1995			WO 9512389	HCAPLUS
Anon	1995			WO 9513289	HCAPLUS
Anon	1995			WO 9529892	HCAPLUS
Anon	1996			WO 9606074	HCAPLUS
Anon	1996			WO 9611209	HCAPLUS
Anon	1997			EP 0780386	HCAPLUS
Anon	1997			WO 9720824	HCAPLUS
Anon	1997			WO 9724117	HCAPLUS
Anon	1997			JP 9749679	
Anon	1998			WO 9837877	HCAPLUS
Anon	1998			WO 9838163	HCAPLUS
Anon	1999			EP 0930067	HCAPLUS
Anon	1999			WO 9909000	HCAPLUS
Anon	1999			WO 9925687	HCAPLUS
Anon	1999			WO 9942436	HCAPLUS
Anon	2000			WO 0046221	HCAPLUS
Anon	2000			WO 0050396	HCAPLUS
Anon	2000			WO 0059874	HCAPLUS
Anon	2000			WO 0069821	HCAPLUS
Barta	2003			US 6541489 B1	HCAPLUS
Barta	1998			U S patent applicati	
Barta	1999			U S patent applicati	
Barta	2000			U S patent applicati	
Barta	2001			U S patent applicati	
Barta	2001			U S patent applicati	
Barta	2002			U S patent applicati	
Bender	1999			US 5932595 A	HCAPLUS
Brown	1998		243	Matrix Metalloprotei	HCAPLUS
Dack	1999				HCAPLUS
Denis	1997	15A	175	Invest New Drugs	

Donald	1986			US 4595700 A	HCAPLUS
Freskos	2000			US 6013649 A	HCAPLUS
Gearing	1994	376	555	Nature	
Kenyon, B	1996	37		A Model of Angiogene	MEDLINE
King	1994		206	Med Chem:Principle a	
Knight	1992	296	263	FEBS Lett	HCAPLUS
Luckow	1993	67	4566	J Virol	HCAPLUS
McClure	1999				HCAPLUS
McGeehan	1994	370	558	Nature	HCAPLUS
Mitchell	1996	97	761	J Clin Invest	HCAPLUS
Rasmussen	1997	75	69	Pharmacol Ther	
Reboul	1996	97	2011	J Clin Invest	HCAPLUS
Schwartz	1992	29	271	Progr Med Chem	HCAPLUS
Takahashi	2001			US 6300514 B1	HCAPLUS
Tang	2001	33	33	The International Jo	HCAPLUS
Woessner	1998		1	Matrix Metalloprotei	

L21 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:991502 HCAPLUS

DOCUMENT NUMBER: 140:28052

TITLE: Asymmetric synthesis of aminopyrrolidinones

INVENTOR(S): Waltermire, Robert E.; Savage, Scott A.; Campagna, Silvio; Magnus, Nicholas A.; Confalone, Pasquale N.; Yates, Matthew; Meloni, David J.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

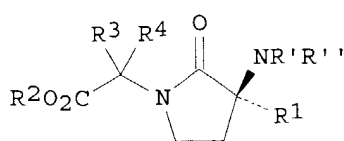
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003104220	A1	20031218	WO 2003-US7969	20030314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003236401	A1	20031225	US 2003-389528	20030314
US 6770763	B2	20040803		

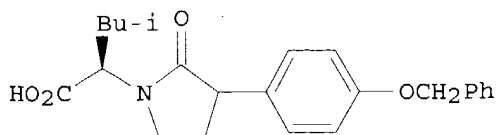
PRIORITY APPLN. INFO.: US 2002-387637P P 20020611

OTHER SOURCE(S): CASREACT 140:28052; MARPAT 140:28052

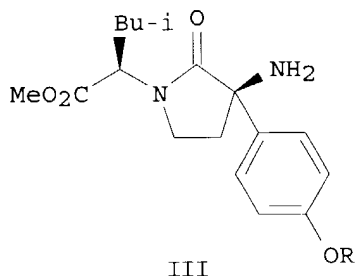
GI



I



II



III

AB A novel process for the asym. synthesis of an aminopyrrolidinones I [R' is H, (cyclo)alkyl; R'' is a group R' or OH; R1 is substituted Ph or pyridyl; R2 is H, alkyl, Ph, benzyl; R3 is H, Q, (oxa)(aza)alk(en)(yn)ylene-Q, where Q is (un)substituted carbocyclyl; R4 is (oxa)(aza)alk(en)(yn)ylene-H] and corresponding aminoazetidinone, aminopiperidinone, and aminohexahydroazepinone analogs involves amination of corresponding pyrrolidinones or analogs. The products are useful as intermediates for MMP and TACE inhibitors. Thus, pyrrolidinone II was prepared by cyclocondensation of p-PhCH2OC6H4CH(CH2CHO)CO2Me with D-leucine Me ester hydrochloride. Amination of II with 1-chloro-1-nitrosocyclopentane, followed by catalytic hydrogenation in MeOH, mesylation, N-protection with p-tolualdehyde, and reaction with 4-(chloromethyl)-2-methylquinoline (R-Cl) afforded III (isolated as the HCl salt).

ED Entered STN: 21 Dec 2003

IC ICM C07D401-10

ICS C07D207-04

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 7, 28

ST aminopyrrolidinone leucine deriv prepn inhibitor TACE **MMP**;
pyrrolidinone amino leucine deriv prepn inhibitor TACE **MMP**

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Kisfaludy	1984			US 4428938	HCAPLUS
Merck & Co Inc	1998			WO 9844797	HCAPLUS

L21 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:875294 HCAPLUS

DOCUMENT NUMBER: 139:364955

TITLE: Preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP**-13

INVENTOR(S): Freeman-cook, Kevin Daniel; Noe, Mark Carl

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091259	A1	20031106	WO 2003-IB1576	20030415
WO 2003091259	C1	20040212		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003225056	A1	20031204	US 2003-423671	20030425
PRIORITY APPLN. INFO.:			US 2002-376157P	P 20020426
OTHER SOURCE(S):			MARPAT 139:364955	

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors (shown as I; variables defined below; e.g. II) and to pharmaceutical compns. and methods of treating inflammation, cancer and other disorders. For I: ; ring X is a 5-7 membered heterocyclic ring; A is (C6-C10)aryl or (C1-C10)heteroaryl; Y = a bond, -O-, -S-, >C=O, >SO2, >S=O, -CH2O-, -OCH2-, -CH2S-, -SCH2-, -CH2SO-, -CH2SO2-, -SOCH2-, -SO2CH2-, >NR14, -[N(R14)]CH2-, -CH2[N(R14)]-, -CH2-, -CH:CH-, -C.tplbond.C-, -[N(R14)]SO2- and -SO2[N(R14)]-; B is (C6-C10)aryl, (C3-C7)cycloalkyl, (C1-C10)heterocyclyl and (C1-C10)heteroaryl; G is -R15(CR16R17)p-; p = 0-4; W is (C1-C4)alkoxy(C1-C4)alkyl, (C3-C7)cycloalkyl, (C6-C10)aryl, (C1-C10)heteroaryl and (C1-C10)heterocyclyl; addnl. details including provisos are given in the claims. General semiquant. statements are made about inhibition of metalloproteinases by I; no data is presented for specific examples of I; some I exhibit selectivity towards **MMP** -13 relative to other metalloproteinases but they are not identified. Although the methods of preparation are not claimed, example preps. of 5 I are included.

ED Entered STN: 07 Nov 2003

IC ICM C07D487-10

ICS A61K031-505; A61P029-00; A61P037-00; A61P019-02; C07D239-00; C07D209-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63

ST triaryl oxy aryl spiro pyrimidinetrione prepn metalloproteinase inhibitor;
MMP13 selective metalloproteinase inhibitor triaryl oxy aryl spiro pyrimidinetrione; inflammation drug triaryl oxy aryl spiro pyrimidinetrione; cancer drug triaryl oxy aryl spiro pyrimidinetrione; pharmaceutical compn triaryl oxy aryl spiro pyrimidinetrione metalloproteinase inhibitor

IT Nervous system, disease

(central; preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

- IT Immunity
Metabolism, animal
Reproduction, animal
(disorder; preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)
- IT Allergy
Allergy inhibitors
Anti-infective agents
Anti-inflammatory agents
Antitumor agents
Cardiovascular agents
Cardiovascular system, disease
Connective tissue, disease
Drug delivery systems
Eye, disease
Human
Immunomodulators
Infection
Inflammation
Kidney, disease
Liver, disease
Neoplasm
Nervous system agents
Respiratory tract, disease
Skin, disease
Stomach, disease
(preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)
- IT Spiro compounds
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)
- IT 175449-82-8, **MMP-13**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**MMP-13**, inhibitors; preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)
- IT 620971-38-2P, 1-[6-[4-[4-(4-Fluorophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620971-44-0P, 4-[2-[4-[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]phenyl]oxazol-4-yl]benzonitrile 620971-47-3P, 3-[2-[4-[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]phenyl]oxazol-4-yl]benzonitrile 620971-50-8P, 1-[6-[4-[4-(2-Fluorophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620971-52-0P, 1-[6-[4-[4-(3-Fluorophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)
- IT 141907-41-7, Matrix metalloproteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT 109-64-8, 1,3-Dibromopropane 403-29-2, 2-Bromo-1-(4-fluorophenyl)ethanone 445-27-2, 1-(2-Fluorophenyl)ethanone 455-36-7, 1-(3-Fluorophenyl)ethanone 540-38-5, 4-Iodophenol 685-87-0, Diethyl bromomalonate 4548-45-2, 2-Chloro-5-nitropyridine 20099-89-2, 4-(2-Bromoacetyl)benzonitrile 50916-55-7, 3-(2-Bromoacetyl)benzonitrile
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT 127426-15-7P, 4-(2-Fluorophenyl)oxazole 620633-04-7P, 4-(4-Fluorophenyl)oxazole 620971-39-3P, 1-[6-[4-[4-(4-Fluorophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620971-40-6P 620971-41-7P, 2-(4-Iodophenoxy)-5-nitropyridine 620971-42-8P, [6-(4-Iodophenoxy)pyridin-3-yl]amine 620971-43-9P 620971-45-1P, 1-[6-[4-[4-(4-Cyanophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620971-46-2P, 4-(Oxazol-4-yl)benzonitrile 620971-48-4P, 1-[6-[4-[4-(3-Cyanophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620971-49-5P, 3-(Oxazol-4-yl)benzonitrile 620971-51-9P, 1-[6-[4-[4-(2-Fluorophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620971-53-1P, 1-[6-[4-[4-(3-Fluorophenyl)oxazol-2-yl]phenoxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620971-54-2P, 4-(3-Fluorophenyl)oxazole
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of triaryl-oxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Blagg, J	2001			WO 0112611 A	HCAPLUS
Scott, B	2002			WO 0234753 A	HCAPLUS

L21 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:875293 HCAPLUS

DOCUMENT NUMBER: 139:364954

TITLE: Preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**

INVENTOR(S): Noe, Mark Carl; Freeman-cook, Kevin Daniel

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091258	A1	20031106	WO 2003-IB1508	20030415
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 US 2004010141 A1 20040115 US 2003-423779 20030425
 PRIORITY APPLN. INFO.: US 2002-376159P P 20020426
 OTHER SOURCE(S): MARPAT 139:364954
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to N-substituted-heteroaryloxy-aryl-spiro-pyrimidine-2,4,6-trione metalloproteinase inhibitors (shown as I; variables defined below; e.g. II) and to pharmaceutical compns. and methods of treating inflammation, cancer and other disorders. For I: ; ring X is a 5-7 membered heterocyclic ring; A is (C6-C10)aryl or (C2-C10)heteroaryl; Y = a bond, -O-, -S-, >C:O, >SO2, >S:O, -CH2O-, -OCH2-, -CH2S-, -SCH2-, -CH2SO-, -CH2SO2-, -SOCH2-, -SO2CH2-, >NR14, -[N(R14)]CH2-, -CH2[N(R14)]-, -CH2-, -CH:CH-, -C.tplbond.C-, -[N(R14)]SO2- and -SO2[N(R14)]-; B is a heterocyclyl containing at least one N atom; wherein one ring N atom of B is bonded to one C atom of G; G is (C1-C6)alkyl or R15-(CR16R17)p-; p = 0-4; addnl. details including provisos are given in the claims. General semiquant. statements are made about inhibition of metalloproteinases by I; no data is presented for specific examples of I; some I exhibit selectivity towards **MMP-13** relative to other metalloproteinases but they are not identified. Although the methods of preparation are not claimed, example prepn. of 4 I are included.

ED Entered STN: 07 Nov 2003

IC ICM C07D487-10
 ICS A61K031-505; A61P037-00; A61P029-00; A61P019-02; C07D239-00;
 C07D209-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63

ST heteroaryloxy aryl spiro pyrimidinetrione prepn metalloproteinase inhibitor; **MMP13** selective metalloproteinase inhibitor
 heteroaryloxy aryl spiro pyrimidinetrione; cancer drug heteroaryloxy aryl spiro pyrimidinetrione; inflammation drug heteroaryloxy aryl spiro pyrimidinetrione; pharmaceutical compn heteroaryloxy aryl spiro pyrimidinetrione metalloproteinase inhibitor

IT Nervous system, disease
 (central; preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT Immunity
 Metabolism, animal
 Reproduction, animal
 (disorder; preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT Allergy
 Allergy inhibitors
 Anti-infective agents
 Anti-inflammatory agents
 Antitumor agents
 Cardiovascular agents
 Cardiovascular system, disease
 Connective tissue, disease
 Drug delivery systems
 Eye, disease

Human
Immunomodulators
Infection
Inflammation
Kidney, disease
Liver, disease
Neoplasm
Nervous system agents
Respiratory tract, disease
Skin, disease
Stomach, disease

(preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT Spiro compounds

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT 175449-82-8, **MMP-13**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**MMP-13**, inhibitors; preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT 620965-06-2P, 1-[6-[[1-(4-Fluorophenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-13-1P, 4-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]indazol-1-yl]benzonitrile 620965-19-7P, 1-[6-[[1-(Pyridin-3-yl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-26-6P, 1-[6-[[1-Methyl-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-33-5P, 1-[6-[[1-Isopropyl-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-35-7P, 1-[6-[[2-Isopropyl-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-36-8P, 4-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]indazol-2-yl]benzonitrile 620965-38-0P, 1-[6-[[2-(2-Hydroxyethyl)-1-oxo-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-39-1P, 1-[6-[[2-(2-Ethoxyethyl)-1-oxo-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-40-4P, 1-[6-[[2-(4-Fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-41-5P, 1-[6-[[1-(4-Fluorophenyl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-42-6P, 1-[6-[[1-(4-Fluorophenyl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-43-7P, 1-[6-[[2-(Pyridin-3-yl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-44-8P, 1-[6-[[2-(4-Fluorophenyl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-45-9P, 1-[6-[[1-(Pyridin-3-yl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-46-0P, 1-[6-[[2-(4-Fluorophenyl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-47-1P, 1-[6-[[1-(4-Fluorophenyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-48-2P, 1-[6-[[1-(4-Fluorophenyl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-49-3P, 6-[7-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-2,3,4,5-tetrahydrobenzo[b]azepin-1-yl]nicotinonitrile 620965-50-6P,

6-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-2,3-dihydroindol-1-yl]nicotinonitrile 620965-51-7P, 1-[6-[[2-(Pyridin-3-yl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-52-8P, 6-[6-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-3,4-dihydro-2H-quinolin-1-yl]nicotinonitrile 620965-53-9P, 1-[6-[[1-(Pyridin-4-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-54-0P, 1-[6-[[1-(Pyridin-3-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-55-1P, 6-[6-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-3,4-dihydro-1H-isoquinolin-2-yl]nicotinonitrile 620965-56-2P, 6-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-1,3-dihydroisoindol-2-yl]nicotinonitrile 620965-57-3P, 6-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]indazol-1-yl]nicotinonitrile 620965-58-4P, 6-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]indazol-2-yl]nicotinonitrile 620965-59-5P, 1-[6-[[2-(Pyridin-4-yl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-60-8P, 1-[6-[[1-(Pyridin-4-yl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-61-9P, 1-[6-[[2-(Pyridin-4-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-62-0P, 1-[6-[[2-(Pyridin-3-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-63-1P, 1-[6-[[1-(Pyridin-4-yl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-64-2P, 1-[6-[[1-(Pyridin-4-yl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-65-3P, 1-[6-[[1-(Pyridin-3-yl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-66-4P, 1-[6-[[1-(Pyridin-4-yl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-67-5P, 1-[6-[[2-(Pyridin-4-yl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-68-6P, 1-[6-[[1-(Pyridin-3-yl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-69-7P, 1-[6-[[2-(p-Tolyl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-70-0P, 1-[6-[[2-(p-Tolyl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-71-1P, 1-[6-[[2-(4-Chlorophenyl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-72-2P, 1-[6-[[2-(4-Chlorophenyl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-73-3P, 1-[6-[[2-(Pyridin-2-yl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-74-4P, 1-[6-[[2-(Pyridin-2-yl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-75-5P, 1-[6-[[2-(3-Methoxypropyl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-76-6P, 1-[6-[[2-(Pyridazin-3-yl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-77-7P, 1-[6-[[1-Isopropyl-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-78-8P, 1-[6-[[1-Isopropyl-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-79-9P, 1-[6-[[2-Isopropyl-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-80-2P, 1-[6-[[2-(Pyridin-2-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-81-3P, 1-[6-[[2-(Pyridazin-3-yl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-82-4P,

1-[6-[(2-Isopropyl-1,2,3,4-tetrahydroisoquinolin-6-yl)oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-83-5P,
1-[6-[[2-(Pyridazin-3-yl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-84-6P,
1-[6-[[2-(3-Methoxypropyl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-85-7P,
1-[6-[[2-(3-Methoxypropyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-86-8P,
1-[6-[[2-(4-Methoxyphenyl)-2H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-87-9P, 1-[6-[(1-Isopropyl-1,2,3,4-tetrahydroquinolin-6-yl)oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-88-0P, 1-[6-[[1-(3-Methoxypropyl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-89-1P, 1-[6-[[1-(Pyridin-2-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-90-4P, 1-[6-[[1-(Pyridazin-3-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-91-5P, 1-[6-[[1-Isopropyl-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-92-6P, 1-[6-[[2-(p-Tolyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-93-7P, 1-[6-[[1-(4-Methoxyphenyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-94-8P, 1-[6-[[2-(4-Chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-95-9P, 4-[6-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-3,4-dihydro-1H-isoquinolin-2-yl]benzonitrile 620965-96-0P, 4-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-2,3-dihydroindol-1-yl]benzonitrile 620965-97-1P, 1-[6-[[1-(4-Methoxyphenyl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-98-2P, 1-[6-[[2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620965-99-3P, 4-[6-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-3,4-dihydro-2H-quinolin-1-yl]benzonitrile 620966-00-9P, 1-[6-[[1-(4-Methoxyphenyl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-01-0P, 4-[7-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-2,3,4,5-tetrahydrobenzo[b]azepin-1-yl]benzonitrile 620966-02-1P, 4-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]-1,3-dihydroisoindol-2-yl]benzonitrile 620966-03-2P, 1-[6-[[1-(4-Chlorophenyl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-04-3P, 1-[6-[[1-(p-Tolyl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-05-4P, 4-[5-[[5-(6,8,10-Trioxo-1,7,9-triazaspiro[4.5]dec-1-yl)pyridin-2-yl]oxy]benzimidazol-1-yl]benzonitrile 620966-06-5P, 1-[6-[[1-(3-Methoxypropyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-07-6P, 1-[6-[[1-(4-Chlorophenyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-08-7P, 1-[6-[[1-(p-Tolyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-09-8P, 1-[6-[[2-(4-Methoxyphenyl)-2,3-dihydro-1H-isoindol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-10-1P, 1-[6-[[1-(Pyridazin-3-yl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-11-2P, 1-[6-[[1-(Pyridin-2-yl)-1,2,3,4-tetrahydroquinolin-6-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-12-3P,

1-[6-[[1-(p-Tolyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-13-4P, 1-[6-[[1-(4-Methoxyphenyl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-14-5P, 1-[6-[[1-(Pyridazin-3-yl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-15-6P, 1-[6-[[1-(Pyridazin-3-yl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-16-7P, 1-[6-[[1-(Pyridazin-3-yl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-17-8P, 1-[6-[[1-(Pyridin-2-yl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-18-9P, 1-[6-[[1-(Pyridin-2-yl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-19-0P, 1-[6-[[1-(Pyridin-2-yl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-20-3P, 1-[6-[[1-(4-Methoxyphenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-21-4P, 1-[6-[[1-(4-Chlorophenyl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-22-5P, 1-[6-[[1-(3-Methoxypropyl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-23-6P, 1-[6-[[1-(3-Methoxypropyl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-24-7P, 1-[6-[[1-(3-Methoxypropyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-25-8P, 1-[6-[[1-(4-Chlorophenyl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-26-9P, 1-[6-[[1-(4-Chlorophenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-27-0P, 1-[6-[[1-(p-Tolyl)-1H-benzimidazol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione 620966-28-1P, 1-[6-[[1-(p-Tolyl)-2,3-dihydro-1H-indol-5-yl]oxy]pyridin-3-yl]-1,7,9-triazaspiro[4.5]decane-6,8,10-trione
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT 141907-41-7, Matrix metalloproteinase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT 108-39-4, m-Cresol, reactions 109-64-8, 1,3-Dibromopropane 685-87-0, Diethyl bromomalonate 1692-25-7, (3-Pyridyl)boronic acid 1765-93-1, 4-Fluorophenylboronic acid 4548-45-2, 2-Chloro-5-nitropyridine 126747-14-6, 4-Cyanophenylboronic acid
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards **MMP-13**)

IT 620965-07-3P, 1-[6-[[1-(4-Fluorophenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620965-08-4P, 2-[[6-[[1-(4-Fluorophenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]amino]malonic acid diethyl ester 620965-09-5P, [6-[[1-(4-Fluorophenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]amine 620965-10-8P, 1-(4-Fluorophenyl)-5-[(5-nitropyridin-2-yl)oxy]-1H-indazole 620965-11-9P, 5-[(5-Nitropyridin-2-yl)oxy]-1H-indazole 620965-12-0P, [2-Methyl-4-[(5-nitropyridin-2-yl)oxy]phenyl]amine 620965-14-2P, 1-[6-[[1-(4-Cyanophenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620965-15-3P, 2-[[6-[[1-(4-Cyanophenyl)-1H-indazol-5-yl]oxy]pyridin-3-yl]amino]malonic acid diethyl ester 620965-16-4P, 4-[5-[(5-Aminopyridin-

2-yl)oxy]indazol-1-yl]benzonitrile 620965-18-6P, 4-[5-[(5-Nitropyridin-2-yl)oxy]indazol-1-yl]benzonitrile 620965-20-0P, 1-[6-[[1-(Pyridin-3-yl)-1H-indazol-5-yl]oxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620965-21-1P, 2-[[6-[[1-(Pyridin-3-yl)-1H-indazol-5-yl]oxy]pyridin-3-yl]amino]malonic acid diethyl ester 620965-23-3P, 5-[(5-Aminopyridin-2-yl)oxy]-1-(pyridin-3-yl)-1H-indazole 620965-24-4P, 5-[(5-Nitropyridin-2-yl)oxy]-1-(pyridin-3-yl)-1H-indazole 620965-27-7P, 1-[6-[(1-Methyl-1H-indazol-5-yl)oxy]pyridin-3-yl]pyrrolidine-2,2-dicarboxylic acid diethyl ester 620965-29-9P, 2-[[6-[(1-Methyl-1H-indazol-5-yl)oxy]pyridin-3-yl]amino]malonic acid diethyl ester 620965-30-2P, 5-[(5-Aminopyridin-2-yl)oxy]-1-methyl-1H-indazole 620965-31-3P, 5-[(5-Nitropyridin-2-yl)oxy]-1-methyl-1H-indazole

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N-substituted-heteroaryloxy-aryl-spiro-pyrimidinetrione metalloproteinase inhibitors selective towards MMP-13)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Blagg, J	2001			WO 0112611 A	HCAPLUS
Scott, B	2002			WO 0234753 A	HCAPLUS

L21 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:818139 HCAPLUS

DOCUMENT NUMBER: 139:307637

TITLE: Synthesis and phytotoxicity of 4-dedimethylaminotetracycline derivatives

INVENTOR(S): Ashley, Robert A.; Hlavka, Joseph J.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 911,861.

CODEN: USXXCO

DOCUMENT TYPE: Patent

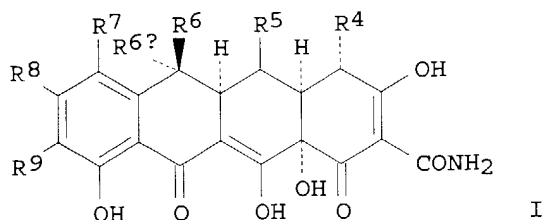
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003195174	A1	20031016	US 2002-274841	20021018
US 6506740	B1	20030114	US 2000-573654	20000518
US 2002160987	A1	20021031	US 2001-911861	20010724
US 6638922	B2	20031028		
PRIORITY APPLN. INFO.:			US 1998-195013	B2 19981118
			US 2000-479604	B2 20000107
			US 2000-573654	A2 20000518
			US 2001-911861	A2 20010724
			US 1998-108948P	P 19981118

OTHER SOURCE(S): MARPAT 139:307637
GI



AB The 4-dedimethylaminotetracycline derivs., such as I [R4 = NOH, N-NH-alkyl, NH-alkyl; R5, R6 = H, OH; R6a = H, Me; R7 = H, (un)substituted amino, NO2, halogen, S(C=S)OEt, N3, acylamino, N2+, CN, OH; R9 = H, (un)substituted amino, NO2, N3, acylamino, OH, S(C=S)OEt, halogen, N2+, RCH(NH2)CO; R = H, alkyl; R8 = H, halogen], and their pharmaceutically acceptable salts were prepared and assayed for their phototoxicity using BALB/c 3T3 (CCL-163) cells. These tetracycline derivs. are claimed for use in the treatment of disorders involving excessive collagen destruction, excessive MT-MMP enzyme activity, excessive TNF activity, excessive nitric oxide activity, excessive IL-1 activity, excessive elastase activity, excessive loss of bone d., excessive protein degradation, excessive muscle wasting, excessive glycosylation of collagen, excessive COX-2 activity, insufficient bone protein synthesis, insufficient interleukin-10 production, excessive phospholipase A2 activity, as well as for treatment of abdominal aortic aneurysm, ulceration of the cornea, periodontal disease, diabetes, diabetes mellitus, scleroderma, progeria, cancer, graft vs. host disease, disease of depressed bone marrow function, thrombocytopenia, prosthetic joint loosening, spondyloarthropathies, osteoporosis, Paget's disease, autoimmune disease, systemic lupus erythematosus and connective tissue disease. 855 These tetracyclines may also be used for treatment of inflammatory conditions, such as inflammatory bowel disease, arthritis, osteoarthritis, rheumatoid arthritis, pancreatitis, nephritis, glomerulonephritis, sepsis, septic shock, lipopolysaccharide endotoxin shock, multisystem organ failure, psoriasis, lung diseases, such as ARDS, cystic fibrosis, emphysema or acute lung injury resulting from inhalation of toxicants, renal diseases, such as chronic or acute renal failure, nephritis or glomerulonephritis, neurodegenerative diseases, such as Alzheimer's disease, Guillain-Barre Syndrome, Krabbe's disease, adrenoleukodystrophy, Parkinson's disease, Huntington's disease, multiple sclerosis, amyotrophic lateral sclerosis, and spongiform encephalopathy. Thus, I (R4, R5, R6, R8, R9 = H; R6a = Me; R7 = NO2) was prepared starting from I (R4, R5, R6, R7, R8, R9 = H; R6a = Me) via nitration.

ED Entered STN: 17 Oct 2003

IC ICM A61K031-65

ICS C07C237-26

NCL 514152000; 552204000

CC 26-6 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1, 63

L21 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:435318 HCAPLUS

DOCUMENT NUMBER: 139:22213

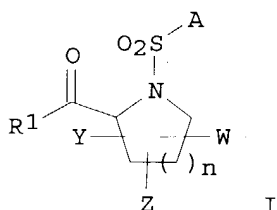
TITLE: Preparation of substituted cyclic amines as
metalloprotease inhibitors

INVENTOR(S): Natchus, Michael George; De, Biswanath; Pikul, Stanislaw; Almstead, Neil Gregory; Bookland, Roger Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 888,675.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003105153	A1	20030605	US 2002-186531	20020701
US 6417219	B1	20020709	US 1997-918317	19970826
US 2002061877	A1	20020523	US 2001-888675	20010625
US 6569855	B2	20030527		
US 2002072517	A1	20020613	US 2001-888759	20010625
US 2003191163	A1	20031009	US 2002-308780	20021203
JP 2004115531	A2	20040415	JP 2003-384116	20031113
US 2004138260	A1	20040715	US 2003-730572	20031208
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			US 1997-918317	A2 19970826
			US 2001-888675	A2 20010625
			US 2001-888759	A2 20010625
			JP 1998-511715	A3 19970822
			US 2002-186531	A2 20020701

OTHER SOURCE(S): MARPAT 139:22213
 GI



AB The invention provides compds. having a structure according to formula (I) [wherein A = each (un)substituted alkyl, heteroalkyl, aryl, heteroaryl; R1 = NHOR2 (where R2 = hydrogen or alkyl); W = H, lower alkyl, or an alkylene bridge that forms a ring in addition to the ring depicted in the formula; Y = HO, SR3, SOR4, SO2R8, alkoxy, (un)substituted NH2; R4 = alkyl, aryl, heteroaryl; R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino; Z = H, HO, alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the ring depicted in the formula; n = 1; provisos given] or pharmaceutically acceptable salts, or biohydrolyzable amides, esters, or imides thereof. These compds. are useful as inhibitors of **metalloproteases**, in particular zinc **metalloprotease**, and effective in treating conditions characterized by excess activity of these enzymes, e.g. degenerative diseases such as arthritis and multiple sclerosis and inflammation (no data). Thus, cis-Hydroxy-D-proline (50 g, 0.38 mol) was dissolved in water:dioxane (1:1, 300 mL) with Et3N (135 mL, 0.96 mol), treated with 4-Methoxyphenylsulfonyl chloride (87 g, 0.42 mol) along with 2,6-dimethylaminopyridine (4.6 g, 0.038 mol), stirred for 14 h at room temperature, concentrated, and diluted with EtOAc to give, after workup, N-(4-Methoxyphenylsulfonyl)-(4R)-hydroxypyrrolidine-(2R)-carboxylic acid.

This intermediate was dissolved in MeOH (500 mL), treated dropwise with 50 mL SOCl₂, stirred for 14 h, evaporated, to dryness, and triturated with CHCl₃ to give N-4-Methoxyphenylsulfonyl-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine as a white solid which was sufficiently pure to carry forward without purification. The latter Me ester (361 mg, 1.15 mmol) was taken in 1 mL MeOH, treated with NH₂OK (1.45 mL, 0.86 M in methanol), and stirred overnight to give, after workup, N-4-Methoxyphenylsulfonyl-(2R)-N-hydroxycarboxamido-(4S)-hydroxypyrrolidine.

ED Entered STN: 06 Jun 2003

IC ICM A61K031-4025

ICS A61K031-401

NCL 514422000; 514423000

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 7, 27

ST cyclic amine prepn **metalloprotease** inhibitor;
hydroxycarboxamidohydroxypyrrolidine prepn **metalloprotease**
inhibitor; hydroxypyrrolidine hydroxycarboxamido prepn
metalloprotease inhibitor; degenerative disease arthritis multiple
sclerosis treatment pyrrolidine prepn; inflammation treatment pyrrolidine
prepn

IT Amines, preparation

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(cyclic; preparation of substituted cyclic amines as **metalloprotease**
inhibitors for treating conditions characterized by excess activity of
these enzymes)

IT Disease, animal

(degenerative; preparation of substituted cyclic amines as
metalloprotease inhibitors for treating conditions
characterized by excess activity of these enzymes)

IT Anti-inflammatory agents

Antiarthritics

Arthritis

Inflammation

Multiple sclerosis

(preparation of substituted cyclic amines as **metalloprotease**
inhibitors for treating conditions characterized by excess activity of
these enzymes)

IT 204071-71-6P, N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-(N-
hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204072-54-8P,
N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)

(intermediate; preparation of substituted cyclic amines as
metalloprotease inhibitors for treating conditions
characterized by excess activity of these enzymes)

IT 1138-54-1P, 4-(Isobutoxy)phenylsulfonyl chloride 57850-07-4P,
N-(4-Methylphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine
203934-42-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-4-
oxopyrrolidine 203934-63-8P 203934-71-8P 203994-66-5P,
N-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-(4R)-hydroxypyrrolidine
203994-80-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine 203994-82-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-**acetylthiopyrrolidine** 204072-15-1P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
benzoyloxypyrrolidine 204072-16-2P, N-(4-Methoxyphenylsulfonyl)-(2S)-
methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-17-3P,

N-(4-Methoxyphenylsulfonyl)-(2S)-methoxycarbonyl-(4S)-hydroxypyrrolidine
204072-18-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-(4S)-
hydroxypyrrolidine 204072-19-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-methoxypyrrolidine 204072-20-8P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
(trifluoromethanesulfonyloxy)pyrrolidine 204072-21-9P 204072-23-1P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[(benzothiazol-2-yl)
thio]pyrrolidine 204072-24-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-[N-methyl-2-**imidazolylthio**]pyrrolidine
204072-25-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[N-
methyl-2-**imidazolylthio**]pyrrolidine 204072-26-4P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-phoxypyrrolidine
204072-27-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(4-
benzyloxyphenoxy)pyrrolidine 204072-28-6P, N-(4-Methoxyphenylsulfonyl)-
(2R)-methoxycarbonyl-(4S)-(3-phenylaminophenoxy)pyrrolidine
204072-29-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-
pyridinyloxy)pyrrolidine 204072-30-0P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-**phenylthiopyrrolidine** 204072-31-1P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
(methanesulfonyloxy)pyrrolidine 204072-32-2P, N-(4-
Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(4-
methoxyphenylthio)pyrrolidine 204072-34-4P, N-(4-
Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-
methoxyphenylthio)pyrrolidine 204072-36-6P, N-(4-
Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-ethoxymethoxypyrrolidine
204072-37-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
benzyloxymethoxypyrrolidine 204072-38-8P, N-(4-Methoxyphenylsulfonyl)-
(2R)-methoxycarbonyl-(4R)-[(2-methoxyethoxy)methoxy]pyrrolidine
204072-39-9P 204072-40-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-carboxy-4-
oxopyrrolidine 204072-41-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4R)-4-hydroxy-4-ethylpyrrolidine 204072-42-4P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-4-hydroxy-4-
phenylpyrrolidine 204072-44-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-3,3-dimethyl-4-oxopyrrolidine 204072-45-7P,
N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-3,3-dimethyl-(4R)-
hydroxypyrrolidine 204072-46-8P, N-(3,4-Dimethoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-47-9P,
N-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine 204072-49-1P, N-(4-Butoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-benzoyloxypyrrolidine 204072-50-4P,
N-(4-Bromobenzenesulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine
204072-51-5P, N-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-methoxycarbonyl-
(4R)-hydroxypyrrolidine 204072-52-6P, N-(2,4-Dichlorophenylsulfonyl)-
(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-53-7P,
4-(2-Methoxyethoxy)phenylsulfonyl chloride 204072-55-9P,
N-(4-Phenoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine
204072-56-0P, N-(4-Isobutyloxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-
hydroxypyrrolidine 204072-57-1P, N-(2-Methyl-4-bromophenylsulfonyl)-(2R)-
methoxycarbonyl-(4S)-(3-**methoxyphenylthio**)pyrrolidine
204072-58-2P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-
benzothiazolylthio)pyrrolidine 204072-59-3P,
N-(2-Nitro-4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-
benzothiazolylthio)pyrrolidine 204072-60-6P,
N-(4-Butoxyphenylsulfonyl)-(2R)-Methoxycarbonyl-(4S)-(4-
methoxyphenylthio)pyrrolidine 204072-61-7P, N-(4-
Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-pyridyloxy)pyrrolidine
204072-62-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-
azidopyrrolidine 204072-64-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-
methoxycarbonyl-(4R)-(methylsulfonyloxy)pyrrolidine 204072-65-1P,
N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-azidopyrrolidine

204072-66-2P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-aminopyrrolidine 204072-67-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-propylaminopyrrolidine 204072-68-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-n-hexylaminopyrrolidine 204072-69-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-phenylethylamino)pyrrolidine 204072-70-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(N-butyl-N-hexylamino)pyrrolidine 204072-71-9P 204072-72-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(methanesulfonyl)amino]pyrrolidine 204072-74-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(3-pyridylmethyl)amino]pyrrolidine 204072-75-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-(3-pyridylmethyl)-N-(methanesulfonyl)amino]pyrrolidine 204072-76-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N,N-bis(methanesulfonyl)amino]pyrrolidine 204072-77-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-(methanesulfonyl)propylamino]pyrrolidine 204072-78-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(4-methoxyphenylsulfonyl)amino]pyrrolidine 204072-79-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-oxohexyl)aminopyrrolidine 204072-81-1P 204072-82-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(2R)-1-oxo-2-benzyloxypropyl]amino]pyrrolidine 204072-83-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[2R)-1-oxo-2-benzyloxy-3-phenylpropyl]amino]pyrrolidine 204072-84-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-benzyloxypropyl]propylamino]pyrrolidine 204072-85-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-hydroxypropyl]propylamino]pyrrolidine 204072-86-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-((2R)-1-oxo-2-benzyloxy-3-phenylpropyl)propylamino]pyrrolidine 204072-87-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-((2R)-1-oxo-2-hydroxy-3-phenylpropyl)propylamino]pyrrolidine 204072-88-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-piperidyl)pyrrolidine 204072-89-9P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-piperidyl)pyrrolidine 204072-90-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-morpholinopyrrolidine 204072-91-3P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-morpholinopyrrolidine 204072-92-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-93-5P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204073-01-8P 204073-02-9P 537704-28-2P 537704-31-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-aminopyrrolidine formate 537704-32-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[N-methyl-3-imidazolyl)sulfonyl]amino]pyrrolidine 537704-35-1P 537704-63-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-66-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-68-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-allyl-2,5-dioxoimidazolidin-3-yl)pyrrolidine 537704-72-6P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,4-dioxo-5,5-dimethylimidazolidin-1-yl)pyrrolidine 537704-74-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(5S)-5-methyl-2,4-dioxoimidazolidin-1-yl]pyrrolidine 537704-76-0P, N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-methoxycarbonyl-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-78-2P, N-(4-

Phenoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted cyclic amines as **metalloprotease** inhibitors for treating conditions characterized by excess activity of these enzymes)

IT 81669-70-7, **Metalloprotease**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation of substituted cyclic amines as **metalloprotease** inhibitors for treating conditions characterized by excess activity of these enzymes)

- IT 203934-18-3P 204071-36-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-38-5P, N-(4-Methoxyphenylsulfonyl)-(2S)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-40-9P, N-(4-Methoxyphenylsulfonyl)-(2S)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-42-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-methoxypyrrolidine 204071-43-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(benzothiazol-2-yl)**thio**]pyrrolidine 204071-44-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-[(benzothiazol-2-yl)**thio**]pyrrolidine 204071-45-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-methyl-2-imidazolyl**thio**]pyrrolidine 204071-46-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-[N-methyl-2-imidazolyl**thio**]pyrrolidine 204071-47-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-phenoxy-pyrrolidine 204071-48-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(4-benzyloxyphenoxy)pyrrolidine 204071-49-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-phenylaminophenoxy)pyrrolidine 204071-50-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-pyridinyloxy)pyrrolidine 204071-51-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-**phenylthiopyrrolidine** 204071-52-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(4-methoxyphenyl**thio**)pyrrolidine 204071-53-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methoxyphenyl**thio**)pyrrolidine 204071-54-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-ethoxymethoxypyrrolidine 204071-55-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-benzyloxymethoxypyrrolidine 204071-56-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-[(2-methoxyethoxy)methoxy]pyrrolidine 204071-57-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-**mercaptopyrrolidine** 204071-58-9P 204071-59-0P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-ethylpyrrolidine 204071-60-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-phenylpyrrolidine 204071-62-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-3,3-dimethyl-(4R)-hydroxypyrrolidine 204071-63-6P, N-(4-Methylphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-64-7P, N-(3,4-Dimethoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-65-8P, N-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-66-9P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-67-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-hydroxypyrrolidine 204071-68-1P, N-(4-Bromobenzenesulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-69-2P, N-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-70-5P,

N-(2,4-Dichlorophenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-72-7P, N-(4-Phenoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-73-8P, N-(4-Isobutyloxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 204071-74-9P, N-(2-Methyl-4-bromophenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methoxyphenylthio)pyrrolidine 204071-75-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-Hydroxycarboxamido)-(4S)-(2-benzothiazolylthio)pyrrolidine 204071-76-1P, N-(2-Nitro-4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2-benzothiazolylthio)pyrrolidine 204071-77-2P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(4-methoxyphenylthio)pyrrolidine 204071-78-3P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-pyridyloxy)pyrrolidine 204071-79-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-aminopyrrolidine 204071-80-7P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-aminopyrrolidine 204071-81-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-propylaminopyrrolidine 204071-82-9P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-n-hexylaminopyrrolidine 204071-83-0P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2-phenylethylamino)pyrrolidine 204071-84-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(N-butyl-N-hexylamino)pyrrolidine 204071-85-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(methanesulfonyl)amino]pyrrolidine 204071-86-3P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(methanesulfonyl)amino]pyrrolidine 204071-88-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(3-pyridylmethyl)-N-(methanesulfonyl)amino]pyrrolidine 204071-89-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N,N-bis(methanesulfonyl)amino]pyrrolidine 204071-90-9P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-(methanesulfonyl)propylamino]pyrrolidine 204071-91-0P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(4-methoxyphenylsulfonyl)amino]pyrrolidine 204071-92-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-oxohexylamino)pyrrolidine 204071-94-3P 204071-95-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(2R)-1-oxo-2-benzyloxypropyl]amino]pyrrolidine 204071-96-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[[2R)-1-oxo-2-benzyloxy-3-phenylpropyl]amino]pyrrolidine 204071-98-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-((2R)-1-oxo-2-hydroxy-3-phenylpropyl)propylamino]pyrrolidine 204071-99-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-00-4P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-01-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-morpholinopyrrolidine 204072-02-6P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-morpholinopyrrolidine 204072-03-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-04-8P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-12-8P 537704-26-0P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-hydroxypyrrolidine 537704-29-3P 537704-34-0P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[[N-methyl-3-imidazolyl]sulfonyl]amino]pyrrolidine 537704-36-2P 537704-43-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[N-[(2R)-1-oxo-2-hydroxypropyl]propylamino]pyrrolidine 537704-65-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-67-9P, N-(4-

Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-69-1P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-allylimidazolidin-3-yl)pyrrolidine 537704-73-7P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,4-dioxo-5,5-dimethylimidazolidin-1-yl)pyrrolidine 537704-75-9P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(5S)-5-methyl-2,4-dioxoimidazolidin-1-yl]pyrrolidine 537704-77-1P, N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-79-3P, N-(4-Phenoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-80-6P, N-(4-Methoxyphenylsulfonyl)-(2R)-hydroxycarboxamido-(4R)-4-hydroxy-4-ethylpyrrolidine 538350-55-9P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted cyclic amines as **metalloprotease** inhibitors for treating conditions characterized by excess activity of these enzymes)

IT 3970-21-6, 2-Methoxyethoxymethyl chloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of substituted cyclic amines as **metalloprotease** inhibitors for treating conditions characterized by excess activity of these enzymes)

IT 204073-03-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted cyclic amines as **metalloprotease** inhibitors for treating conditions characterized by excess activity of these enzymes)

IT 60-56-0, 2-Mercapto-1-methylimidazole 65-85-0, Benzoic acid, reactions 74-88-4, Methyl iodide, reactions 75-08-1, **Ethanethiol** 77-71-4, 5,5-Dimethylhydantoin 98-58-8, 4-Bromobenzenesulfonyl chloride 98-59-9, p-Toluenesulfonyl chloride 98-68-0, 4-Methoxyphenylsulfonyl chloride 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 100-58-3, Phenylmagnesium bromide 101-18-8, 3-Hydroxydiphenylamine 103-16-2, 4-(Benzyloxy)phenol 108-98-5, **Thiophenol**, reactions 109-00-2, 3-Hydroxypyridine 111-26-2, Hexylamine 111-30-8, Glutaric dialdehyde 122-78-1, Phenylacetaldehyde 123-38-6, Propionaldehyde, reactions 124-63-0, Methanesulfonyl chloride 140-66-9, 4-Octylphenol 142-61-0, Hexanoyl chloride 149-30-4, 2-Mercaptobenzothiazole 149-87-1 334-88-3, Diazomethane 358-23-6 500-22-1, 3-Pyridinecarboxaldehyde 507-09-5, **Thioacetic acid**, reactions 616-04-6, 1-Methylhydantoin 624-83-9, Methyl isocyanate 627-42-9 696-63-9, 4-Methoxythiophenol 925-90-6, Ethylmagnesium bromide 1138-56-3, p-Butoxyphenylsulfonyl chloride 1499-56-5, trans-4-Hydroxy-L-proline methyl ester 1623-92-3, 4-Phenoxyphenylsulfonyl chloride 2051-62-9, 1,1'-Biphenyl-4-yl chloride 2584-71-6, cis-4-Hydroxy-D-proline 3366-93-6, 1-Allylhydantoin 3587-60-8, Benzyl chloromethyl ether 5414-19-7, 2-Bromoethyl ether 6482-24-2, 2-Bromoethyl methyl ether 7326-19-4, D-3-Phenyllactic acid 7617-67-6, Bis(2-bromoethyl) sulfone 15570-12-4, 3-Methoxythiophenol 16271-33-3, 2,4-Dichlorobenzenesulfonyl chloride 18092-54-1 23095-31-0, 3,4-Dimethoxyphenylsulfonyl chloride 40856-73-3 51212-37-4 54571-66-3 81102-38-7, cis-4-Hydroxy-L-proline methyl ester 100836-85-9 114676-47-0 139937-37-4, 2-Methyl-4-bromobenzenesulfonyl chloride 182937-63-9, (2R)-2-Benzyloxy-3-phenylpropanoic acid 537704-27-1 537704-33-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of substituted cyclic amines as
metalloprotease inhibitors for treating conditions
characterized by excess activity of these enzymes)

L21 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:154246 HCAPLUS

DOCUMENT NUMBER: 138:187764

TITLE: Preparation of 2-(azacycylcarbonylamino)thiazoles as
tyrosine kinase inhibitors

INVENTOR(S): Hartman, George D.; Tucker, Thomas J.; Sisko, John T.;
Smith, Anthony M.; Lumma, William C., Jr.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

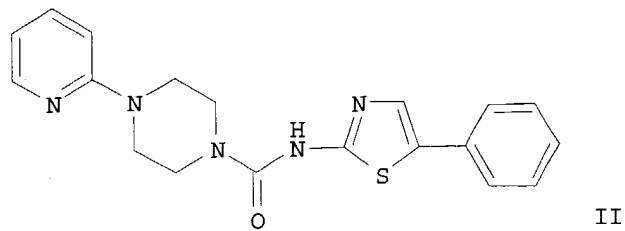
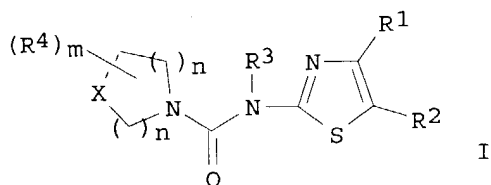
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015778	A1	20030227	WO 2002-US27156	20020813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004192926	A1	20040930	US 2004-486574	20040211
PRIORITY APPLN. INFO.:			US 2001-313234P	P 20010817
			WO 2002-US27156	W 20020813
OTHER SOURCE(S):		MARPAT 138:187764		
GI				



AB Title ureas I [wherein X = CH or NR3a; m = 1-6; n = independently 0-2; R1 = H, halo, alkyl, or alkoxy; R2 = (un)substituted aryl, CN, CONRaRb, halo, cycloalkyl, or C.tplbond.CRC; R3 = H, alkyl, SO2Rd, CORd, or CO2Rd; R3a = per the definition of R3 or substituted alkyl; R4 = H, alkylene-NR5R6, CO2H, CO2Rd, halo, OH, alkoxy, or (un)substituted alkyl; R5 and R6 = independently H, alkyl, SO2Rd, CO2Rd, CORd, alkylene-NRaRb, alkylene-CONRaRb, or (un)substituted alkylene-heterocyclyl or aryl; or NR5R6 = (un)substituted heterocyclyl; Ra and Rb = independently H, (cyclo)alkyl, Ph, CO2Rd, CORd, or SO2Rd; Rc = H, Ph, or alkyl; Rd = Ph or alkyl; or pharmaceutically acceptable salts or stereoisomers thereof] were prepared for the inhibition, regulation, and/or modulation tyrosine kinase signal transduction. For example, reaction of 2-[(4-nitrophenoxy-carbonyl)amino]-5-phenylthiazole with 4-(2-pyridyl)piperazine in the presence of DIEA in DMF at 60° for 1 h gave II. Tested I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.01 - 5.0 µM. I are useful for the treatment of tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).

ED Entered STN: 28 Feb 2003

IC ICM A61K031-427

ICS A61K031-4439; A61K031-506; A61K031-5377; C07D417-12; C07D417-14

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT 9028-35-7, HMG-CoA reductase 9068-38-6, Reverse transcriptase 39391-18-9, Cyclooxygenase 131384-38-8, Prenyltransferase 141907-41-7, Matrix **metalloprotease** 144114-21-6, HIV protease 329900-75-6, COX 2

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor, combination therapy agent; preparation of (azacycylcarbonylamino)thiazole tyrosine kinase inhibitors as angiogenesis inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Pharmacia & Upjohn S P	2000			WO 0026203 A1	HCAPLUS

L21 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:905716 HCAPLUS

DOCUMENT NUMBER: 138:11438

TITLE: Use of compounds with combined NEP/MP-inhibitory activity in the preparation of medicaments

INVENTOR(S): Berger, Claudia; Fischer, Yvan; Hoeltje, Dagmar; Waldeck, Harald; Weske, Michael; Ziegler, Dieter

PATENT ASSIGNEE(S): Solvay Pharmaceuticals GmbH, Germany

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094176	A2	20021128	WO 2002-EP5259	20020514
WO 2002094176	A3	20031211		

W: AU, BR, CA, CN, CZ, DZ, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PH,

PL, RU, SK, UA, US, ZA
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, TR
 EP 1397141 A2 20040317 EP 2002-743004 20020514
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY, TR
 BR 2002009855 A 20040615 BR 2002-9855 20020514
 US 2004162345 A1 20040819 US 2003-715112 20031118
 PRIORITY APPLN. INFO.: EP 2001-112231 A 20010518
 US 2001-292337P P 20010522
 WO 2002-EP5259 W 20020514

OTHER SOURCE(S): MARPAT 138:11438

AB This invention relates to the use of a compound having combined, in particular concurrent, inhibitors activity on neutral endopeptidase (NEP) and on a novel **metalloprotease** (MP) designated IGS5, or of a pharmaceutically acceptable salt or solvate or biolabile ester thereof, for the manufacture of a medicament (pharmaceutical composition) for treating a larger mammal, preferably a human, suffering from or being susceptible to a disease or condition which can be alleviated or prevented by combined or concurrent inhibition of NEP and IGS5. In a particular aspect the present invention pertains to the use of said compds. with combined or concurrent NEP/IGS5 inhibitory activity for treating a larger mammal, preferably a human, suffering from or being susceptible to a disease or condition where big-ET-1 levels are elevated and which disease or condition can be alleviated or prevented by combined or concurrent inhibition of NEP and IGS5. In a further particular aspect the present invention pertains to the use of said compds. with combined or concurrent NEP/IGS5 inhibitory activity for treating a larger mammal, preferably a human, suffering from or being susceptible to a disease or condition where ET-1 is significantly upregulated and which disease or condition can be alleviated or prevented by combined or concurrent inhibition of NEP and IGS5. In the present invention said compds. with combined or concurrent NEP/IGS5-inhibitory activity preferably are used for the treatment and/or prophylaxis of hypertension, including secondary forms of hypertension such as renal or pulmonary hypertension, heart failure, angina pectoris, arrhythmias, myocardial infarction, cardiac hypertrophy, cerebral ischemia, peripheral vascular disease, subarachnoidal hemorrhage, chronic obstructive pulmonary disease (COPD), asthma, renal disease, atherosclerosis, and pain in colorectal cancer or prostate cancer, in mammals, preferably in humans, and more preferably in a patient sub-population suffering from or being susceptible to a disease or condition which can be alleviated or prevented by combined or concurrent inhibition of NEP and IGS5. Furthermore, it may be beneficial to addnl. combine the said compds. showing combined or concurrent NEP/IGS5 inhibitory activity with other individual and/or combined **metalloprotease** inhibitors than the NEP/IGS5 inhibitors, e.g. with sep. ACE- and/or NEP-inhibitors and/or mixed inhibitors of these **metalloproteases**.

ED Entered STN: 29 Nov 2002

IC ICM A61K

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

IT 36357-77-4, Phosphoramidon 76721-89-6, **Thiorphan**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(therapeutic use of compds. with combined NEP/MP-inhibitory activity)

L21 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:540272 HCAPLUS

DOCUMENT NUMBER: 137:109216

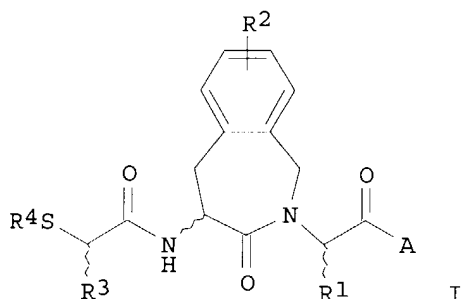
TITLE: Preparation of N-carboxymethylbenzolactams as matrix

INVENTOR(S): metalloproteinase inhibitors
 Warshawsky, Alan M.; Janusz, Michael J.; Flynn, Gary A.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 41 pp., Cont. of U.S. Ser. No. 465,737, abandoned.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002095035	A1	20020718	US 2002-77913	20020220
US 6544980	B2	20030408		

PRIORITY APPLN. INFO.:
 US 1998-172244P P 19981231
 US 1999-465737 B1 19991217

OTHER SOURCE(S): MARPAT 137:109216
 GI



AB A method of inhibiting matrix metalloproteinases comprises administration of title compds. [I; A = OH, NRR'; R, R' = H, alkyl; NRR' = morpholino, piperidino, pyrrolidino, N-isoindolyl; R1 = alkyl, (CH2)4NH2, CH2OH, CH(OH)Me, etc.; R2 = H, halo, alkoxy, etc.; R3 = alkyl, (CH2)mW, (CH2)pAr, etc.; m = 2-8; p = 0-10; W = phthalimido; Ar = pyridyl, thienyl, quinolinyl, etc.; R4 = H, COR10, CO(CH2)qK, SG; R10 = H, alkyl, Ph, CH2Ph; q = 0-2; K = pyridyl, imidazolyl, etc.; G = pyridyl, (CH2)w(pyridyl), etc.; w = 1-3] (no data). Thus, tert-Bu 2-(4-amino-3-oxo-1,3,4,5-tetrahydrobenzo[c]azepin-2-yl)-4-methylvalerate, (S)-3-phenyl-2-benzoylthiopropionic acid, and EEDQ were stirred 18 h in CH2Cl2 to give 85% amide, which was stirred with CF3CO2H and anisole in CH2Cl2 to give 2-[4-(2-benzoylthio-2-phenylpropionylamino)-3-oxo-1,3,4,5-tetrahydrobenzo[c]azepin-2-yl]-4-methylvaleric acid.

ED Entered STN: 19 Jul 2002

IC ICM A61K031-55

NCL 540523000

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1, 34

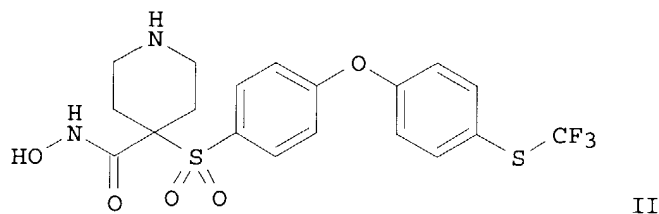
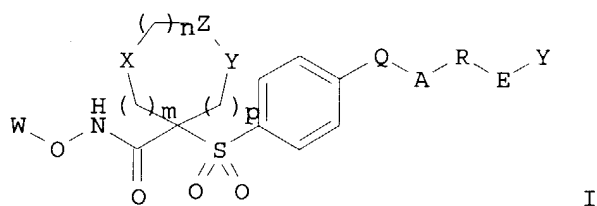
IT 141907-41-7, Matrix **metalloprotease**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; preparation of N-carboxymethylbenzolactams as matrix metalloproteinase inhibitors)

L21 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:824220 HCAPLUS
DOCUMENT NUMBER: 134:17399
TITLE: Aromatic sulfone hydroxamic acid
metalloprotease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.;
Boehm, Terri L.; Carroll, Jeffrey N.; Decrescenzo,
Gary A.; Fobian, Yvette M.; Freskos, John N.; Getman,
Daniel P.; McDonald, Joseph J.; Hockerman, Susan L.;
Howard, Susan C.; Kolodziej, Stephen A.; Li, Madeleine
Hui; Mischke, Deborah A.; Rico, Joseph G.; Stehle,
Nathan W.; Tollefson, Michael B.; Vernier, William F.;
Villamil, Clara I.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 616 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069821	A1	20001123	WO 2000-US6719	20000515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6750228	B1	20040615	US 2000-570731	20000512
CA 2372934	AA	20001123	CA 2000-2372934	20000515
EP 1183239	A1	20020306	EP 2000-930088	20000515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010562	A	20030610	BR 2000-10562	20000515
JP 2003520196	T2	20030702	JP 2000-618238	20000515
AU 766792	B2	20031023	AU 2000-47970	20000515
NZ 515217	A	20040430	NZ 2000-515217	20000515
ZA 2001009006	A	20021202	ZA 2001-9006	20011031
NO 2001005543	A	20020110	NO 2001-5543	20011113
PRIORITY APPLN. INFO.:				
			US 1999-311837	A 19990514
			US 2000-570731	A 20000512
			US 1997-66007P	P 19971114
			US 1998-95347P	P 19980804
			US 1998-101080P	P 19980918
			US 1999-256948	B2 19990224
			WO 2000-US6719	W 20000515
OTHER SOURCE(S): MARPAT 134:17399				
GI				



AB A treatment process is disclosed that comprises administering an effective amount of an aromatic sulfone hydroxamic acid I [W = H, cation, certain acyl or **thioacyl** groups; m, n, p = 0-2; (m+n+p) = 1 to 4; one of X, Y, and Z = CO, NH or derivs., O, S, SO, SO₂, etc., and the other two = (un)substituted CH₂; or XZ or ZY = (un)substituted NHCO, NHSO, NHSO₂, SS, OCO, etc., and the other one = (un)substituted CH₂; or n = 0 and XZY = atoms to complete various N/O/S heterocycles; Q = 5- to 7-membered heterocycle with 1-2 N atoms, one bound to Ph, and with -AREY bound in para-type positions; A = bond, O, S, (un)substituted NH, COO, OCO, CH:CH, C.tplbond.C, N:N, NHNH, NHCOO, (un)substituted CONH, NHCO, etc.; R = alkylene, arylene, heteroarylene, etc., with provisos; E = bond, CONH, NHCO, CO, SO₂, NHSO₂, SO₂NH, S, etc.; Y = absent, H, alkyl, alkoxy, aryl, aryloxy, heteroaryl, etc.] to a host having a condition associated with pathol. matrix **metalloprotease** (MMP) activity. I exhibit excellent inhibitory activity of one or more **MMP** enzymes, such as **MMP-2**, **MMP-9** and **MMP-13**, while exhibiting substantially less inhibition of (at least) **MMP-1**. Also disclosed are **metalloprotease** inhibitor compds. having such selective activities, processes for manufacture of such compds., and pharmaceutical compns. using such inhibitors. The compds. are potentially useful against a wide variety of conditions, notably as antiinflammatory, antiangiogenesis, and antitumor agents. Over 900 example compds. are listed, most with supporting phys. data, and many with synthetic details. For instance, Et N-(tert-butoxycarbonyl)-4-(4-fluorophenylsulfonyl)-4-piperidinecarboxylate (preparation given) was subjected to a sequence of: (1) etherification with 4-(CF₃S)C₆H₄OH (100%); (2) alkaline hydrolysis of the ester (100%); (3) amidation with THP-ONH₂ (45%); and (4) acid deprotection of the THP ether (40%), to give title compound II.HCl. The latter salt selectively inhibited **MMP-13** with IC₅₀ 0.2 nM, and **MMP-2** with IC₅₀ 0.1 nM, but with IC₅₀ >10,000 nM against **MMP-1**.

ED Entered STN: 24 Nov 2000

IC ICM C07D211-66

ICS C07D405-12; C07D405-14; C07D309-08; C07D335-02; C07D409-12;
C07D401-06; C07D401-12; A61K031-445; A61K031-4523; A61P009-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 7

ST arom sulfone hydroxamic acid prepn matrix **metalloprotease** inhibitor; **MMP** inhibitor prepn hydroxamic acid pyran

thiopyran piperidine
IT Angiogenesis inhibitors
Anti-inflammatory agents
Antitumor agents
(preparation of aromatic sulfone hydroxamic acids as **metalloprotease** inhibitors)
IT Hydroxamic acids
Sulfones
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aromatic sulfone hydroxamic acids as **metalloprotease** inhibitors)
IT 9001-12-1, **MMP**-1 141907-41-7, Matrix **metalloprotease** 146480-35-5, **MMP** 2 146480-36-6, **MMP** 9 175449-82-8, **MMP**-13
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(binding; preparation of aromatic sulfone hydroxamic acids as **metalloprotease** inhibitors)
IT 308822-81-3P 308822-82-4P 308822-86-8P 308822-95-9P 308823-05-4P
308824-05-7P 308824-24-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of aromatic sulfone hydroxamic acids as **metalloprotease** inhibitors)
IT 226390-98-3P 226391-00-0P 226391-03-3P 226391-36-2P 226391-57-7P
226391-61-3P 226392-57-0P 226392-69-4P 226393-71-1P 226393-73-3P
226393-97-1P 226393-99-3P 226396-25-4P 226396-28-7P 289486-35-7P
289486-36-8P 308821-65-0P 308821-66-1P 308821-67-2P 308821-69-4P
308821-71-8P 308821-72-9P 308821-73-0P 308821-74-1P 308821-75-2P
308821-76-3P 308821-77-4P 308821-79-6P 308821-81-0P 308821-82-1P
308821-83-2P 308821-85-4P 308821-87-6P 308821-89-8P 308821-91-2P
308821-93-4P 308821-95-6P 308821-96-7P 308821-97-8P 308821-98-9P
308821-99-0P 308822-00-6P 308822-01-7P 308822-02-8P 308822-03-9P
308822-04-0P 308822-05-1P 308822-06-2P 308822-07-3P 308822-08-4P
308822-09-5P 308822-11-9P 308822-13-1P 308822-14-2P 308822-16-4P
308822-17-5P 308822-18-6P 308822-19-7P 308822-21-1P 308822-22-2P
308822-23-3P 308822-24-4P 308822-26-6P 308822-28-8P 308822-29-9P
308822-30-2P 308822-31-3P 308822-32-4P 308822-33-5P 308822-34-6P
308822-35-7P 308822-36-8P 308822-38-0P 308822-41-5P 308822-42-6P
308822-44-8P 308822-45-9P 308822-46-0P 308822-49-3P 308822-51-7P
308822-53-9P 308822-54-0P 308822-56-2P 308822-58-4P 308822-60-8P
308822-63-1P 308822-64-2P 308822-66-4P 308822-69-7P 308822-71-1P
308822-72-2P 308822-73-3P 308822-74-4P 308822-75-5P 308822-77-7P
308822-78-8P 308822-79-9P 308822-80-2P 308822-83-5P 308822-84-6P
308822-85-7P 308822-87-9P 308822-88-0P 308822-89-1P 308822-90-4P
308822-91-5P 308822-92-6P 308822-93-7P 308822-94-8P 308822-96-0P
308822-97-1P 308822-98-2P 308822-99-3P 308823-00-9P 308823-01-0P
308823-02-1P 308823-03-2P 308823-04-3P 308823-06-5P 308823-07-6P
308823-08-7P 308823-09-8P 308823-10-1P 308823-11-2P 308823-12-3P
308823-13-4P 308823-14-5P 308823-15-6P 308823-16-7P 308823-17-8P
308823-18-9P 308823-19-0P 308823-20-3P 308823-21-4P 308823-22-5P
308823-23-6P 308823-24-7P 308823-25-8P 308823-26-9P 308823-27-0P
308823-28-1P 308823-29-2P 308823-30-5P 308823-31-6P 308823-32-7P
308823-33-8P 308823-34-9P 308823-35-0P 308823-36-1P 308823-37-2P
308823-38-3P 308823-39-4P 308823-40-7P 308823-41-8P 308823-42-9P
308823-43-0P 308823-44-1P 308823-45-2P 308823-46-3P 308823-47-4P

308823-48-5P	308823-49-6P	308823-50-9P	308823-51-0P	308823-52-1P
308823-53-2P	308823-54-3P	308823-55-4P	308823-56-5P	308823-57-6P
308823-58-7P	308823-59-8P	308823-60-1P	308823-61-2P	308823-62-3P
308823-63-4P	308823-64-5P	308823-65-6P	308823-66-7P	308823-67-8P
308823-68-9P	308823-69-0P	308823-70-3P	308823-71-4P	308823-72-5P
308823-73-6P	308823-74-7P	308823-75-8P	308823-76-9P	308823-77-0P
308823-78-1P	308823-79-2P	308823-80-5P	308823-81-6P	308823-82-7P
308823-83-8P	308823-84-9P	308823-85-0P	308823-86-1P	308823-87-2P
308823-91-8P	308823-92-9P	308823-93-0P	308823-94-1P	308823-95-2P
308823-96-3P	308823-97-4P	308823-98-5P	308823-99-6P	308824-00-2P
308824-01-3P	308824-02-4P	308824-03-5P	308824-04-6P	308824-06-8P
308824-07-9P	308824-08-0P	308824-09-1P	308824-10-4P	308824-11-5P
308824-12-6P	308824-13-7P	308824-14-8P	308824-15-9P	308824-16-0P
308824-17-1P	308824-18-2P	308824-19-3P	308824-20-6P	308824-21-7P
308824-22-8P	308824-23-9P	308824-25-1P	308824-26-2P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)

IT	308824-27-3P	308824-28-4P	308824-29-5P	308824-30-8P	308824-31-9P
	308824-32-0P	308824-33-1P	308824-34-2P	308824-35-3P	308824-36-4P
	308824-37-5P	308824-38-6P	308824-39-7P	308824-40-0P	308824-41-1P
	308824-42-2P	308824-43-3P	308824-44-4P	308824-45-5P	308824-46-6P
	308824-47-7P	308824-48-8P	308824-49-9P	308824-50-2P	308824-51-3P
	308824-52-4P	308824-53-5P	308824-54-6P	308824-55-7P	308824-56-8P
	308824-57-9P	308824-58-0P	308824-59-1P	308824-60-4P	308824-61-5P
	308824-62-6P	308824-63-7P	308824-64-8P	308824-65-9P	308824-66-0P
	308824-69-3P	308824-71-7P	308824-73-9P	308824-75-1P	308824-77-3P
	308824-79-5P	308824-81-9P	308824-83-1P	308824-85-3P	308824-86-4P
	308824-87-5P	308824-88-6P	308824-89-7P	308824-90-0P	308824-91-1P
	308824-92-2P	308824-93-3P	308824-94-4P	308824-95-5P	308824-96-6P
	308824-97-7P	308824-98-8P	308824-99-9P	308825-00-5P	308825-01-6P
	308825-02-7P	308825-03-8P	308825-04-9P	308825-05-0P	308825-06-1P
	308825-07-2P	308825-08-3P	308825-09-4P	308825-10-7P	308825-11-8P
	308825-12-9P	308825-13-0P	308825-14-1P	308825-15-2P	308825-16-3P
	308825-17-4P	308825-18-5P	308825-19-6P	308825-20-9P	308825-21-0P
	308825-22-1P	308825-23-2P	308825-24-3P	308825-25-4P	308825-26-5P
	308825-27-6P	308825-28-7P	308825-29-8P	308825-30-1P	308825-31-2P
	308825-32-3P	308825-33-4P	308825-34-5P	308825-35-6P	308825-36-7P
	308825-37-8P	308825-38-9P	308825-39-0P	308825-40-3P	308825-41-4P
	308825-42-5P	308825-43-6P	308825-44-7P	308825-45-8P	308825-46-9P
	308825-47-0P	308825-48-1P	308825-49-2P	308825-50-5P	308825-51-6P
	308825-52-7P	308825-53-8P	308825-54-9P	308825-55-0P	308825-56-1P
	308825-57-2P	308825-58-3P	308825-59-4P	308825-60-7P	308825-61-8P
	308825-62-9P	308825-63-0P	308825-64-1P	308825-65-2P	308825-66-3P
	308825-67-4P	308825-68-5P	308825-69-6P	308825-70-9P	308825-71-0P
	308825-72-1P	308825-73-2P	308825-74-3P	308825-76-5P	308825-78-7P
	308825-79-8P	308825-80-1P	308825-81-2P	308825-83-4P	308825-85-6P
	308825-86-7P	308825-87-8P	308825-88-9P	308825-89-0P	308825-90-3P
	308825-92-5P	308825-93-6P	308825-94-7P	308825-95-8P	308825-96-9P
	308825-97-0P	308825-98-1P	308825-99-2P	308826-00-8P	308826-01-9P
	308826-02-0P	308826-04-2P	308826-05-3P	308826-06-4P	308826-07-5P
	308826-08-6P	308826-09-7P	308826-10-0P	308826-11-1P	308826-12-2P
	308826-13-3P	308826-14-4P	308826-15-5P	308826-16-6P	308826-17-7P
	308826-18-8P	308826-19-9P	308826-20-2P	308826-21-3P	308826-23-5P
	308826-25-7P	308826-26-8P	308826-27-9P	308826-28-0P	308826-29-1P
	308826-30-4P	308826-31-5P	308826-32-6P	308826-34-8P	308826-36-0P
	308826-37-1P	308826-39-3P	308826-41-7P	308826-43-9P	308826-44-0P
	308826-45-1P	308826-46-2P	308826-47-3P	308826-48-4P	308826-49-5P

308826-50-8P	308826-51-9P	308826-52-0P	308826-53-1P	308826-54-2P
308826-55-3P	308826-57-5P	308826-58-6P	308826-59-7P	308826-60-0P
308826-61-1P	308826-62-2P	308826-63-3P	308826-64-4P	308826-65-5P
308826-66-6P	308826-67-7P	308826-69-9P	308826-70-2P	308826-71-3P
308826-72-4P	308826-73-5P	308826-74-6P	308826-75-7P	308826-76-8P
308826-77-9P	308826-78-0P	308826-80-4P	308826-82-6P	308826-83-7P
308826-84-8P	308826-85-9P	308826-86-0P	308826-88-2P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as metalloprotease inhibitors)

IT	308826-90-6P	308826-92-8P	308826-93-9P	308826-94-0P	308826-95-1P
	308826-96-2P	308826-97-3P	308826-98-4P	308826-99-5P	308827-00-1P
	308827-01-2P	308827-02-3P	308827-03-4P	308827-04-5P	308827-05-6P
	308827-06-7P	308827-07-8P	308827-08-9P	308827-09-0P	308827-10-3P
	308827-11-4P	308827-12-5P	308827-13-6P	308827-14-7P	308827-15-8P
	308827-16-9P	308827-17-0P	308827-18-1P	308827-19-2P	308827-20-5P
	308827-21-6P	308827-22-7P	308827-23-8P	308827-24-9P	308827-25-0P
	308827-26-1P	308827-27-2P	308827-28-3P	308827-29-4P	308827-30-7P
	308827-32-9P	308827-33-0P	308827-34-1P	308827-35-2P	308827-36-3P
	308827-37-4P	308827-38-5P	308827-39-6P	308827-40-9P	308827-41-0P
	308827-42-1P	308827-43-2P	308827-44-3P	308827-45-4P	308827-46-5P
	308827-47-6P	308827-48-7P	308827-49-8P	308827-50-1P	308827-51-2P
	308827-52-3P	308827-53-4P	308827-54-5P	308827-55-6P	308827-56-7P
	308827-57-8P	308827-58-9P	308827-59-0P	308827-60-3P	308827-61-4P
	308827-62-5P	308827-63-6P	308827-64-7P	308827-65-8P	308827-66-9P
	308827-67-0P	308827-68-1P	308827-69-2P	308827-70-5P	308827-72-7P
	308827-74-9P	308827-75-0P	308827-77-2P	308827-78-3P	308827-79-4P
	308827-80-7P	308827-81-8P	308827-82-9P	308827-83-0P	308827-84-1P
	308827-85-2P	308827-86-3P	308827-87-4P	308827-88-5P	308827-89-6P
	308827-90-9P	308827-91-0P	308827-92-1P	308827-93-2P	308827-94-3P
	308827-95-4P	308827-96-5P	308827-97-6P	308827-98-7P	308827-99-8P
	308828-00-4P	308828-01-5P	308828-02-6P	308828-03-7P	308828-04-8P
	308828-05-9P	308828-06-0P	308828-07-1P	308828-08-2P	308828-09-3P
	308828-10-6P	308828-11-7P	308828-12-8P	308828-13-9P	308828-14-0P
	308828-15-1P	308828-16-2P	308828-17-3P	308828-18-4P	308828-19-5P
	308828-20-8P	308828-21-9P	308828-22-0P	308828-23-1P	308828-24-2P
	308828-25-3P	308828-26-4P	308828-27-5P	308828-28-6P	308828-29-7P
	308828-30-0P	308828-31-1P	308828-33-3P	308828-34-4P	308828-35-5P
	308828-36-6P	308828-37-7P	308828-39-9P	308828-40-2P	308828-41-3P
	308828-42-4P	308828-43-5P	308828-44-6P	308828-45-7P	308828-46-8P
	308828-47-9P	308828-48-0P	308828-49-1P	308828-50-4P	308828-51-5P
	308828-52-6P	308828-53-7P	308828-54-8P	308828-55-9P	308828-56-0P
	308828-57-1P	308828-58-2P	308828-59-3P	308828-60-6P	308828-61-7P
	308828-62-8P	308828-63-9P	308828-64-0P	308828-65-1P	308828-66-2P
	308828-68-4P	308828-69-5P	308828-70-8P	308828-71-9P	308828-72-0P
	308828-73-1P	308828-74-2P	308828-75-3P	308828-76-4P	308828-77-5P
	308828-78-6P	308828-79-7P	308828-80-0P	308828-81-1P	308828-82-2P
	308828-83-3P	308828-84-4P	308828-85-5P	308828-86-6P	308828-87-7P
	308828-88-8P	308828-89-9P	308828-90-2P	308828-91-3P	308828-92-4P
	308828-93-5P	308828-94-6P	308828-95-7P	308828-96-8P	308828-97-9P
	308828-98-0P	308828-99-1P	308829-00-7P	308829-01-8P	308829-02-9P
	308829-03-0P	308829-04-1P	308829-05-2P	308829-06-3P	308829-07-4P
	308829-08-5P	308829-09-6P	308829-10-9P	308829-11-0P	308829-12-1P
	308829-13-2P	308829-14-3P	308829-15-4P	308829-16-5P	308829-17-6P
	308829-19-8P	308829-20-1P	308829-21-2P	308829-23-4P	308829-24-5P
	308829-25-6P	308829-26-7P	308829-27-8P	308829-28-9P	308829-29-0P
	308829-32-5P	308829-34-7P	308829-35-8P	308829-36-9P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as **metalloprotease** inhibitors)

IT	308829-37-0P	308829-38-1P	308829-39-2P	308829-40-5P	308829-41-6P
	308829-42-7P	308829-43-8P	308829-44-9P	308829-45-0P	308829-46-1P
	308829-47-2P	308829-48-3P	308829-49-4P	308829-51-8P	308829-53-0P
	308829-54-1P	308829-55-2P	308829-56-3P	308829-57-4P	308829-58-5P
	308829-59-6P	308829-60-9P	308829-61-0P	308829-62-1P	308829-63-2P
	308829-64-3P	308829-65-4P	308829-66-5P	308829-67-6P	308829-68-7P
	308829-69-8P	308829-70-1P	308829-71-2P	308829-72-3P	308829-73-4P
	308829-74-5P	308829-75-6P	308829-76-7P	308832-77-1P	308832-78-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of aromatic sulfone hydroxamic acids as **metalloprotease** inhibitors)

IT	405-31-2P	4783-86-2P	81151-35-1P	84358-13-4P	113113-66-9P
	138647-49-1P	142851-03-4P	162881-76-7P	180695-79-8P	188527-08-4P
	192329-80-9P	192330-49-7P	193022-95-6P	195503-42-5P	226388-52-9P
	226388-56-3P	226388-60-9P	226389-21-5P	226389-49-7DP, resin-bound	
	226389-52-2P	226391-07-7DP, resin-bound	226395-65-9P	226395-75-1P	
	226395-93-3P	226396-02-7P	226396-03-8P	226396-33-4P	226396-34-5P
	226396-40-3P	226396-42-5P	226396-44-7P	226396-51-6P	226396-53-8P
	226396-54-9P	226396-56-1P	226396-62-9P	226396-63-0P	226396-64-1P
	226396-65-2P	226396-66-3P	226396-67-4P	226396-70-9P	226396-71-0P
	226396-72-1P	226397-96-2P	226398-02-3P	226398-13-6P	226399-44-6P
	226399-45-7P	226399-47-9P	226399-49-1P	226399-50-4P	226399-52-6P
	226399-90-2P	226399-91-3P	226399-92-4P	226399-95-7P	226400-29-9P
	226400-78-8P	226400-79-9P	226400-80-2P	226401-17-8P	226401-18-9P
	226401-19-0P	226401-21-4P	226401-22-5P	226401-23-6P	226401-67-8P
	226401-76-9P	287954-32-9P	308798-39-2P	308823-36-1DP, resin-bound	
	308823-46-3DP, resin-bound		308823-88-3P	308823-89-4P	308823-90-7P
	308829-77-8DP, resin-bound		308829-78-9P	308829-79-0DP, resin-bound	
	308829-80-3DP, resin-bound		308829-81-4DP, resin-bound	308829-82-5P	
	308829-83-6P	308829-84-7P	308829-85-8P	308829-87-0P	308829-88-1P
	308829-89-2P	308829-90-5P	308829-91-6P	308829-92-7P	308829-93-8P
	308829-94-9P	308829-95-0P	308829-96-1P	308829-97-2P	308829-98-3P
	308829-99-4P	308830-00-4P	308830-01-5P	308830-02-6P	308830-03-7P
	308830-04-8P	308830-05-9P	308830-07-1P	308830-09-3P	308830-11-7P
	308830-13-9P	308830-15-1P	308830-17-3P	308830-19-5P	308830-20-8P
	308830-22-0P	308830-24-2P	308830-26-4P	308830-29-7P	308830-30-0P
	308830-32-2P	308830-34-4P	308830-36-6P	308830-38-8P	308830-39-9P
	308830-41-3P	308830-43-5P	308830-45-7P	308830-47-9P	308830-49-1P
	308830-50-4P	308830-51-5P	308830-52-6P	308830-53-7P	308830-54-8P
	308830-55-9P	308830-56-0P	308830-57-1P	308830-58-2P	308830-59-3P
	308830-60-6P	308830-61-7P	308830-62-8P	308830-63-9P	308830-64-0P
	308830-65-1P	308830-66-2P	308830-67-3P	308830-68-4P	308830-69-5P
	308830-70-8P	308830-71-9P	308830-72-0P	308830-73-1P	308830-74-2P
	308830-75-3P	308830-76-4P	308830-77-5P	308830-78-6P	308830-79-7P
	308830-80-0P	308830-81-1P	308830-82-2P	308830-83-3P	308830-84-4P
	308830-85-5P	308830-86-6P	308830-87-7P	308830-88-8P	308830-89-9P
	308830-90-2P	308830-91-3P	308830-92-4P	308830-93-5P	308830-94-6P
	308830-95-7P	308830-96-8P	308830-97-9P		

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of aromatic sulfone hydroxamic acids as **metalloprotease** inhibitors)

IT	51-45-6, Histamine, reactions	62-53-3, Aniline, reactions	67-62-9, Methoxyamine	75-04-7, Ethylamine, reactions	78-81-9, Isobutylamine
----	-------------------------------	-----------------------------	-----------------------	--------------------------------	------------------------

90-04-0 95-51-2, 2-Chloroaniline 96-34-4, Methyl 2-chloroacetate
 98-09-9, Benzenesulfonyl chloride 98-16-8, 3-(Trifluoromethyl)aniline
 98-88-4, Benzoyl chloride 99-89-8, 4-Isopropylphenol 99-98-9,
 N,N-Dimethyl-p-phenylenediamine 100-07-2, 4-Anisoyl chloride 100-39-0,
 Benzyl bromide 100-46-9, Benzylamine, reactions 100-61-8,
 N-Methylaniline, reactions 103-67-3, N-Benzylmethylamine 103-71-9,
 Phenyl isocyanate, reactions 103-76-4, N-(2-Hydroxyethyl)piperazine
 103-80-0, Phenylacetyl chloride 104-12-1, 4-Chlorophenyl isocyanate
 104-81-4, 4-Methylbenzyl bromide 104-94-9 106-38-7, 4-Bromotoluene
 106-96-7, Propargyl bromide 107-08-4, 1-Iodopropane 107-10-8,
 1-Propylamine, reactions 108-00-9, N,N-Dimethylethylenediamine
 108-42-9, 3-Chloroaniline 108-95-2, Phenol, reactions 108-98-5,
Thiophenol, reactions 109-00-2, 3-Hydroxypyridine 109-01-3,
 1-Methylpiperazine 109-85-3, 2-Methoxyethylamine 109-89-7,
 Diethylamine, reactions 109-90-0, Ethyl isocyanate 110-85-0,
 Piperazine, reactions 110-89-4, Piperidine, reactions 110-91-8,
 Morpholine, reactions 110-96-3, Diisobutylamine 111-49-9 111-95-5
 122-04-3, 4-Nitrobenzoyl chloride 122-99-6, Ethylene glycol phenyl ether
 123-75-1, Pyrrolidine, reactions 123-90-0, **Thiomorpholine**
 124-02-7 124-40-3, Dimethylamine, reactions 141-43-5, Ethanolamine,
 reactions 142-25-6, N,N,N'-Trimethylethylenediamine 150-76-5,
 4-Methoxyphenol 156-87-6, 3-Amino-1-propanol 288-32-4, Imidazole,
 reactions 288-88-0, 1H-1,2,4-Triazole 312-94-7, 2-
 (Trifluoromethyl)benzoyl chloride 329-01-1, 3-(Trifluoromethyl)phenyl
 isocyanate 329-15-7, 4-(Trifluoromethyl)benzoyl chloride 348-54-9,
 2-Fluoroaniline 371-40-4, 4-Fluoroaniline 371-41-5, 4-Fluorophenol
 371-42-6, 4-(Fluoro)**thiophenol** 372-19-0, 3-Fluoroaniline
 393-52-2, 2-Fluorobenzoyl chloride 395-44-8, 2-(Trifluoromethyl)benzyl
 bromide 402-23-3, 3-(Trifluoromethyl)benzyl bromide 402-45-9,
 α,α,α -Trifluoro-p-cresol 403-43-0, 4-Fluorobenzoyl
 chloride 404-71-7, 3-Fluorophenyl isocyanate 407-25-0, Trifluoroacetic
 anhydride 421-83-0, Trifluoromethanesulfonyl chloride 455-14-1,
 4-(Trifluoromethyl)aniline 459-46-1, 4-Fluorobenzyl bromide 461-82-5,
 4-(Trifluoromethoxy)aniline 461-84-7, 4-(**Trifluoromethylthio**
)phenol 496-15-1, Indoline 498-94-2, Isonipecotic acid 504-24-5,
 4-Aminopyridine 527-69-5, 2-Furoyl chloride 536-90-3 556-61-6,
 Methyl **isothiocyanate** 591-54-8, 4-Aminopyrimidine 592-55-2,
 2-Bromoethyl ethyl ether 616-45-5, 2-Pyrrolidinone 620-13-3,
 3-Methylbenzyl bromide 622-95-7, 4-Chlorobenzyl bromide 625-43-4,
 N-Methylisobutylamine 626-56-2, 3-Methylpiperidine 626-64-2,
 4-Hydroxypyridine 627-37-2, N-Methylallylamine 658-46-8 694-05-3,
 1,2,3,6-Tetrahydropyridine 753-90-2, 2,2,2-Trifluoroethylamine
 777-44-6, 3-(Trifluoromethyl)benzenesulfonyl chloride 828-27-3,
 p-(Trifluoromethoxy)phenol 874-60-2, 4-Toluoyl chloride 877-88-3,
 3,5-Dimethoxybenzyl bromide 877-96-3, 1-[3-(Dimethylamino)propyl]piperaz
 ine 929-06-6, 2-(2-Aminoethoxy)ethanol 933-88-0, 2-Toluoyl chloride
 1008-91-9, 1-(4-Pyridyl)piperazine 1011-15-0, 1-(2-
 Fluorophenyl)piperazine 1013-76-9, 1-(2,4-Dimethylphenyl)piperazine
 1126-09-6, Ethyl isonipecotate 1195-45-5, 4-Fluorophenyl isocyanate
 1423-27-4 1535-73-5, 3-(Trifluoromethoxy)aniline 1535-75-7,
 2-(Trifluoromethoxy)aniline 1548-13-6, 4-(Trifluoromethyl)phenyl
 isocyanate 1632-84-4, 4-(**Methylthio**)phenyl isocyanate
 1645-65-4, 4-(Trifluoromethyl)phenyl **isothiocyanate** 1711-05-3,
 3-Anisoyl chloride 1711-07-5, 3-Fluorobenzoyl chloride 1939-99-7,
 α -Toluenesulfonyl chloride 2033-89-8, 3,4-Dimethoxyphenol
 2038-57-5, Benzenepropanamine 2131-64-8, 4-(Dimethylamino)phenyl
isothiocyanate 2251-50-5, Pentafluorobenzoyl chloride
 2251-65-2, 3-(Trifluoromethyl)benzoyl chloride 2252-63-3,
 1-(4-Fluorophenyl)piperazine 2338-18-3 2516-47-4,
 (Aminomethyl)cyclopropane 2836-04-6, N,N-Dimethyl-1,3-phenylenediamine

2971-79-1, Methyl isonipecotate 2991-42-6, 4-(Trifluoromethyl)benzenesulfonyl chloride 3173-56-6, Benzyl isocyanate 3202-33-3, 4-Phenoxy piperidine 3282-30-2, Pivaloyl chloride 3535-37-3, 3,4-Dimethoxybenzoyl chloride 3644-18-6, 1-[2-(Dimethylamino)ethyl]piperazine 3647-69-6, 4-(2-Chloroethyl)morpholine hydrochloride 3731-51-9, 2-(Aminomethyl)pyridine 3731-52-0, 3-(Aminomethyl)pyridine 3731-53-1, 4-(Aminomethyl)pyridine 4023-34-1, Cyclopropanecarbonyl chloride 4124-31-6, Trichloroacetic anhydride 4318-37-0, 1-Methylhomopiperazine 4318-42-7 4597-87-9, 2-(Methylamino)pyridine 4693-91-8, 4-Methoxyphenylacetyl chloride 4755-50-4, 4-(Dimethylamino)benzoyl chloride 4892-89-1, 1-(2-Morpholinoethyl)piperazine 5181-06-6, 1-(2-Methoxyphenyl)piperidine 5271-67-0, 2-**Thiophenecarbonyl** chloride 5292-43-3, tert-Butyl bromoacetate 5321-49-3, 1-(2-Phenylethyl)piperazine 5382-16-1, 4-Hydroxypiperidine 5414-19-7, Bis-(2-bromoethyl) ether 5638-76-6, 2-[2-(Methylamino)ethyl]pyridine 6269-89-2, 1-(4-Nitrophenyl)piperazine 6457-49-4, 4-(Hydroxymethyl)piperidine 6482-24-2, 2-Bromoethyl methyl ether 6485-55-8, cis-2,6-Dimethylmorpholine 6640-24-0, 1-(3-Chlorophenyl)piperazine 6711-48-4, 3,3'-Iminobis(N,N-dimethylpropylamine) 6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)hydroxylamine 7357-67-7, 3-Morpholinopropyl chloride 7377-26-6, Methyl 4-(chlorocarbonyl)benzoate 7379-35-3, 4-Chloropyridine hydrochloride 10111-08-7, 2-Imidazolecarboxaldehyde 10400-19-8, Nicotinoyl chloride 13339-01-0, 1-(2-Ethoxyphenyl)piperazine 13349-82-1, 1-[2-(2-Hydroxyethoxy)ethyl]piperazine 13484-40-7, 1-(2-Methoxyethyl)piperazine 13889-98-0, 1-Acetylpiperazine 13961-36-9, 1-Allylpiperazine 14254-57-0, Isonicotinoyl chloride 14446-75-4, cis-3,5-Dimethylpiperidine 15268-31-2, 3-Pyridyl isocyanate 16413-26-6, 3-Cyanophenyl isocyanate 16744-98-2, 2-Fluorophenyl isocyanate 17201-43-3, 4-Cyanobenzyl bromide 17213-57-9, 3,5-Dimethoxybenzoyl chloride 17452-27-6 17739-45-6, 2-(2-Bromoethoxy)tetrahydro-2H-pyran 18880-04-1, 3,4-Dichlorobenzyl bromide 19853-09-9, 2-Phenylbenzyl bromide 20662-53-7 20980-22-7, 2-(1-Piperazinyl)pyrimidine 21043-40-3, 1-Cyclopentylpiperazine 21615-34-9, 2-Anisoyl chloride 21655-48-1, cis-2,6-Dimethylpiperazine 26389-60-6, N-Propylcyclopropanemethylamine 27129-86-8, 3,5-Dimethylbenzyl bromide 27374-25-0, [(1-Ethoxycyclopropyl)oxy]trimethylsilane 27757-85-3, 2-**Thiophenemethylamine** 30459-17-7, 1-[4-(Trifluoromethyl)phenyl]piperazine 32452-46-3, trans-3,5-Dimethylpiperidine 32459-62-4, 4-Ethoxyphenyl isocyanate 32813-24-4, 2-Piperidinoethyl **isothiocyanate** 33403-97-3, 4-(Ethylaminomethyl)pyridine 34803-66-2, 1-(2-Pyridyl)piperazine 34803-68-4, 1-(2-Pyrazinyl)piperazine 35161-71-8, N-Methylpropargylamine 35309-20-7, 3-Isocyanatopropionic acid 35386-24-4, 1-(2-Methoxyphenyl)piperazine 35730-09-7, 2,5-Difluorobenzoyl chloride 35794-11-7, 3,5-Dimethylpiperidine 35947-12-7, 1-(4-Methoxyphenyl)-2-methylpiperazine 36823-88-8, 4-(Trifluoromethoxy)benzoyl chloride 37517-81-0, Methyl malonyl chloride 38778-05-1, 4-(Phenoxy)**benzenethiol** 39512-50-0, 1-(2-Chlorophenyl)piperazine 39546-32-2, Isonipecotamide 39890-45-4, N-[2-(1-Piperazinyl)acetyl]pyrrolidine 40004-08-8, 1-(Ethoxycarbonylmethyl)piperazine 40172-95-0, 1-(2-Furoyl)piperazine 45597-00-0, cis-3,5-Dimethylmorpholine 49647-20-3, 4-Acetylphenyl isocyanate 50824-05-0, 4-(Trifluoromethoxy)benzyl bromide 51639-48-6 53460-46-1, 1,3,3-Trimethyl-6-azabicyclo[3.2.1]octane 54288-70-9, 4-Bromopiperidine hydrobromide 56346-57-7, 4-(4-Fluorobenzoyl)piperidine 56651-60-6, 4-Methoxybenzyl isocyanate 58315-38-1, N-[2-Nitro-4-(trifluoromethyl)phenyl]piperazine 58333-75-8, 4-(2-Methoxyphenyl)piperidine 63224-35-1, 2-Morpholinoethyl **isothiocyanate** 68337-15-5, 4-(1,2,4-Triazol-1-yl)phenol

68832-13-3 69628-75-7, 1-(1-Phenylethyl)piperazine 76362-12-4,
 4-(4-Methoxybenzoyl)piperidine 76835-20-6, 1-(5-Chloro-2-
 methylphenyl)piperazine 79099-07-3 82911-69-1, N-(9-
 Fluorenylmethoxycarbonyloxy)succinimide 85118-01-0, 3,4-Difluorobenzyl
 bromide 85275-45-2 87394-63-6, 1-[3-(Trifluoromethyl)pyrid-2-
 yl]piperazine 103008-51-1, 2-(Trifluoromethoxy)benzenesulfonyl chloride
 109384-19-2 115761-79-0, 1-(2,4-Difluorophenyl)piperazine 118708-88-6,
 1-[4-(Trifluoromethyl)-2-pyridyl]piperazine 120104-92-9 132834-59-4,
 1-[3-Chloro-5-(trifluoromethyl)pyrid-2-yl]piperazine 159689-88-0,
 3-(Trifluoromethoxy)benzyl bromide 175277-80-2 179756-91-3,
 1-[4-(Trifluoromethyl)-2-pyrimidyl]piperazine 226400-27-7 308830-98-0
 RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

IT 308830-99-1 308831-00-7, 4-(3,5-Dimethylphenoxy)piperidine 308831-01-8
 RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of aromatic sulfone hydroxamic acids as
metalloprotease inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
American Cyanamid Co	1998			WO 9837877 A	HCAPLUS
American Cyanamid Co	1999			WO 9942436 A	HCAPLUS
Ciba Geigy Ag	1994			EP 0606046 A	HCAPLUS
Crescenzo Gary A de	1999			WO 9925687 A	HCAPLUS
Rhone Poulenc Rorer Pha	1997			WO 9724117 A	HCAPLUS

L21 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:535102 HCAPLUS

DOCUMENT NUMBER: 133:150908

TITLE: Preparation of acetylenic α -amino acid-based
 sulfonamide hydroxamic acid TACE inhibitors

INVENTOR(S): Levin, Jeremy Ian; Chen, James Ming; Cole, Derek Cecil

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 293 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044709	A2	20000803	WO 2000-US1981	20000127
WO 2000044709	A3	20001221		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356299	AA	20000803	CA 2000-2356299	20000127
EP 1144368	A2	20011017	EP 2000-905750	20000127
EP 1144368	B1	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

BR 2000007752	A	20011204	BR 2000-7752	20000127
TR 200102132	T2	20020121	TR 2001-200102132	20000127
JP 2002535382	T2	20021022	JP 2000-595966	20000127
AU 766717	B2	20031023	AU 2000-27384	20000127
NZ 511928	A	20031128	NZ 2000-511928	20000127
AT 271035	E	20040715	AT 2000-905750	20000127
ZA 2001004326	A	20020826	ZA 2001-4326	20010525
NO 2001003674	A	20010924	NO 2001-3674	20010726
BG 105738	A	20020531	BG 2001-105738	20010726
PRIORITY APPLN. INFO.:			US 1999-238255	A 19990127
			WO 2000-US1981	W 20000127

OTHER SOURCE(S): MARPAT 133:150908

AB Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO₂, P(O)R₁₀, where R₁₀ = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH₂, S; R₁ = H, aryl, alkyl, alkenyl, alkynyl; R₂ = any group given for R₁, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R₁ and R₂ may form a ring; R₃ = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R₁ and R₃ may form a ring; R₄, R₅ = H, alkyl, CN, C.tplbond.CH; R₆ = any group given for R₁, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepared as inhibitors of TNF- α converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-methylbutyramide was prepared and showed IC₅₀ = 7.4 nM for inhibition of TACE.

ED Entered STN: 04 Aug 2000

IC ICM C07C311-00

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 9001-12-1, **MMP**-1 146480-36-6, **MMP** 9 151769-16-3,Tace 175449-82-8, **MMP**-13

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of acetylenic α -amino acid-based sulfonamide hydroxamic acid TACE inhibitors)

IT 52-67-5, D-Penicillamine 55-22-1, Isonicotinic acid, reactions
 59-67-6, Nicotinic acid, reactions 60-24-2, 2-Mercaptoethanol
 62-57-7, 2-Aminoisobutyric acid 74-11-3 79-03-8, Propionyl chloride
 88-10-8, Diethylcarbamoyl chloride 88-13-1, 3-Thiophenecarboxylic acid 98-68-0, 4-Methoxybenzenesulfonyl chloride 98-89-5, Cyclohexanecarboxylic acid 100-09-4, p-Anisic acid 103-71-9, Phenyl isocyanate, reactions 103-82-2, Phenylacetic acid, reactions 104-03-0, p-Nitrophenylacetic acid 104-94-9, p-Anisidine 106-54-7, 4-Chlorobenzenethiol 106-93-4, 1,2-Dibromoethane 106-96-7, Propargyl bromide 107-08-4, Propyl iodide 107-92-6, Butyric acid, reactions 108-95-2, Phenol, reactions 109-01-3, 1-Methylpiperazine 109-02-4, 4-Methylmorpholine 109-64-8, 1,3-Dibromopropane 109-70-6, 1-Bromo-3-chloropropane 110-65-6, 2-Butyne-1,4-diol 111-77-3, Di(ethylene glycol)mono methyl ether 112-35-6, Tri(ethylene glycol)mono methyl ether 112-80-1, Oleic acid, reactions 123-75-1, Pyrrolidine, reactions 137-00-8, 4-Methyl-5-thiazoleethanol 140-10-3, reactions 288-32-4, Imidazole, reactions 319-78-8, D-Isoleucine 349-88-2, 4-Fluorobenzenesulfonyl chloride 371-40-4 454-29-5, **Homocysteine** 501-52-0, Hydrocinnamic acid 507-19-7, 2-Bromo-2-methylpropane 513-38-2, 1-Iodo-2-Methylpropane 516-06-3, Valine 579-75-9, o-Anisic acid 586-76-5 589-15-1, p-Bromobenzyl bromide 617-27-6, DL-Alanine ethyl ester hydrochloride 623-33-6, Glycine ethyl ester hydrochloride 627-18-9, 1-Bromo-3-propanol 636-44-2, 2,5-Dimethyl-3-furoic acid 637-59-2, 1-Bromo-3-phenylpropane 764-01-2, 2-Butyn-1-ol 825-90-1,

4-Hydroxybenzenesulfonic acid sodium salt 921-01-7, D-Cysteine
 928-90-5, 5-Hexyn-1-ol 1002-36-4, 2-Heptyn-1-ol 1192-63-8,
 1-Pyrrolidinecarbonyl chloride 1445-73-4, 1-Methyl-4-piperidone
 1504-58-1, 3-Phenyl-2-propyn-1-ol 2104-89-4, DL-Serine methyl ester
 2510-36-3, 3,5-Dimethylisoxazole-4-carboxylic acid 2577-48-2, L-Proline
 methyl ester 2949-22-6, Ethyl isocyanatoacetate 2955-88-6,
 1-(2-Hydroxyethyl)pyrrolidine 3031-68-3, 2,4-Hexadiyne-1,6-diol
 3042-81-7, Methyl α -bromophenylacetate 3355-28-0, 1-Bromo-2-butyne
 3445-11-2, 1-(2-Hydroxyethyl)-2-pyrrolidinone 3612-20-2,
 1-Benzyl-4-piperidone 3647-69-6 4285-42-1, n-Methyl-n-phenylcarbamoyl
 chloride 4530-20-5 5271-67-0, 2-Thiophenecarbonyl chloride
 5292-43-3, tert-Butyl bromoacetate 5350-93-6, 5-Amino-2-chloropyridine
 5390-04-5, 4-Pentyn-1-ol 5619-05-6, DL-Valine methyl ester hydrochloride
 5807-30-7, 3,4-Dichlorophenylacetic acid 6261-22-9, 2-Pentyn-1-ol
 6480-68-8, 3-Quinolinecarboxylic acid 6940-78-9, 1-Bromo-4-chlorobutane
 6959-48-4, 3-Picolyl chloride hydrochloride 7051-34-5,
 (Bromomethyl)cyclopropane 10465-81-3, 1,1'-(Azodicarbonyl)dipiperidine
 14316-06-4, D-Alanine methyl ester hydrochloride 14328-64-4
 15159-40-7, 4-Morpholinecarbonyl chloride 15260-83-0 15788-16-6,
 5-Benzimidazolecarboxylic acid 16837-14-2 19009-39-3,
 Diisopropylcarbamoyl chloride 19225-92-4, 1-Methyl-2-
 chloromethylimidazole 19686-73-8, 1-Bromo-2-propanol 22818-40-2
 24091-92-7 26690-80-2 26782-71-8, D-tert-Leucine 31608-23-8
 34010-15-6, cis-11-Tetradecen-1-ol 34297-27-3, D-Penicillamine methyl
 ester hydrochloride 34893-92-0, 3,5-Dichlorophenyl isocyanate
 37993-32-1 40365-61-5, 2-(3-Butynyloxy)tetrahydro-2h-pyran 41345-53-3,
 2,4-Pentadiyn-1-ol 41994-51-8, 1,2,3,4-Tetrahydro-3-
 isoquinolinecarboxylic acid hydrochloride 52605-49-9, Sarcosine ethyl
 ester hydrochloride 57561-39-4 58885-58-8 59337-89-2, 3-
Chlorothiophene-2-carboxylic acid 60421-23-0 68641-49-6,
 Bis(2-oxo-3-oxazolidinyl)phosphinic chloride 77279-24-4 86606-04-4
 89032-21-3 89941-07-1, Ethyl 2-piperazinecarboxylate 91142-50-6
 101469-92-5 108895-85-8 117439-65-3, Cyclohexanecarboxylic acid,
 α -amino-1- **mercapto**- 138542-11-7 161315-62-4
 183673-71-4 206550-68-7 211381-51-0 287406-78-4 287406-80-8
 287406-81-9 287406-82-0 287406-83-1 287406-95-5 287407-02-7
 287407-71-0 287407-95-8 287408-04-2 287408-05-3 287408-06-4
 287408-07-5 287408-08-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of acetylenic α -amino acid-based sulfonamide hydroxamic
 acid TACE inhibitors)

L21 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:475659 HCAPLUS

DOCUMENT NUMBER: **133:104976**

TITLE: 1-Carboxymethyl-2-oxo-azepan derivatives as selective
 inhibitors of **MMP-12**

INVENTOR(S): Warshawsky, Alan M.; Janusz, Michael J.

PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040577	A1	20000713	WO 1999-US26748	19991112
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,				

CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2356689 AA 20000713 CA 1999-2356689 19991112

EP 1150975 A1 20011107 EP 1999-961647 19991112

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

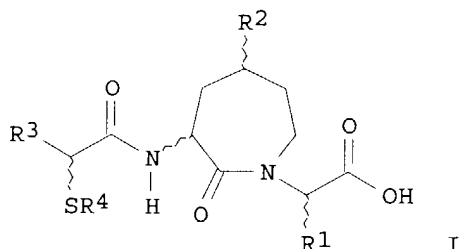
PRIORITY APPLN. INFO.:

US 1998-224457 A 19981231

WO 1999-US26748 W 19991112

OTHER SOURCE(S): MARPAT 133:104976

GI



AB The title compds. [I; R1 = H, alkyl, CH₂SCH₂NHCOMe, etc.; R2 = alkyl, (CH₂)pheteroaryl, (CH₂)pAr1 (wherein Ar1 = (un)substituted Ph, naphthyl); R3 = alkyl, (CH₂)mW, (CH₂)mZQ (W = phthalimido; Z = a bond, O, NR₆, etc.; Q = H, (CH₂)nY; Y = H, aryl, heteroaryl, etc.); R4 = H, COR7, CO(CH₂)qK, SG (K = morpholino, piperidino, pyrrolidino, etc.; G = pyridyl, (CH₂)w(pyridyl), etc.); R6 = H, alkyl; R7 = H, alkyl, (CH₂)pAr2 (Ar2 = (un)substituted Ph, naphthyl); m = 2-4; n = 0-4; p = 0-2; w = 1-3] were claimed as inhibitors of matrix metalloproteinases (**MMPs**), especially as selective inhibitors of **MMP-12** (no data for final compds.). Compds. I are claimed to be effective at 1-100 mg/kg/day.

ED Entered STN: 14 Jul 2000

IC ICM C07D403-12

ICS A61K031-55; C07D223-10

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

ST carboxymethyloxazepan intermediate prepn **MMP12** selective inhibitor

IT 9004-06-2, **MMP 12**

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(1-carboxymethyl-2-oxo-azepan derivs. as selective inhibitors of **MMP-12**)

IT 60-32-2, 6-Aminohexanoic acid 2916-68-9, 2-(Trimethylsilyl)ethanol 22509-74-6, N-Carboethoxyphthalimide 90719-32-7, (S)-4-Benzyl-2-oxazolidinone 143365-54-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(1-carboxymethyl-2-oxo-azepan derivs. as selective inhibitors of **MMP-12**)

IT 4443-26-9P 5107-16-4P 205391-14-6P 205391-15-7P 205391-16-8P
205391-17-9P 205391-18-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(1-carboxymethyl-2-oxo-azepan derivs. as selective inhibitors of
MMP-12)

IT 205391-19-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(1-carboxymethyl-2-oxo-azepan derivs. as selective inhibitors of
MMP-12)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Hoechst Marion Roussel	1998			WO 9812211 A	HCAPLUS

L21 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:475647 HCAPLUS

DOCUMENT NUMBER: 133:104975

TITLE: Preparation of N-carboxymethyl substituted
benzolactams as inhibitors of matrix metalloproteinase

INVENTOR(S): Warshawsky, Alan; Janusz, Michael J.; Flynn, Gary A.

PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 108 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

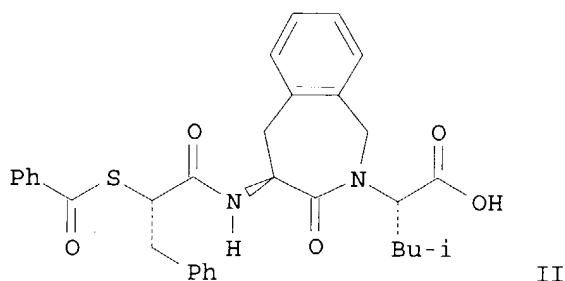
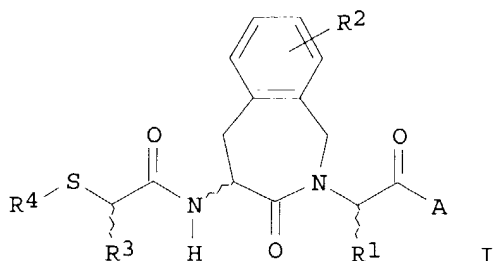
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040564	A1	20000713	WO 1999-US28339	19991130
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358955	AA	20000713	CA 1999-2358955	19991130
EP 1150957	A1	20011107	EP 1999-961877	19991130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-224549 A 19981231
WO 1999-US28339 W 19991130

OTHER SOURCE(S): MARPAT 133:104975

GI



AB The title compds. [I; A = OH, NRR' (wherein R, R' = H, alkyl; NRR' = morpholino, piperidino, pyrrolidino, N-isoindolyl); R1 = alkyl, (CH₂)₄NH₂, CH₂OH, etc.; R2 = H, halo, alkoxy, etc.; R3 = alkyl, (CH₂)_mW, (CH₂)_pAr₃, etc. (m = 2-8; p = 0-10; W = phthalimido; Ar₃ = pyridyl, thienyl, quinolinyl, etc.); R4 = H, COR₁₀, CO(CH₂)_qK, SG (R₁₀ = H, alkyl, Ph, CH₂Ph; q = 0-2; K = pyridyl, 1-imidazolyl, etc.; G = pyridyl, (CH₂)_w(pyridyl), etc.; w = 1-3)] which inhibit matrix metallo-proteinases (**MMPs**) (no biol. data) and as such are useful in treating neoplasms, atherosclerosis, and chronic inflammatory diseases, were prepared E.g., a multi-step synthesis of benzolactam II was given. Compds. I are effective at 1-100 mg/kg/day.

ED Entered STN: 14 Jul 2000

IC ICM C07D223-16

ICS C07D403-12; C07K005-06; A61K031-55; A61P011-00; A61P007-00; A61P035-00

CC 27-21 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
E R Squibb & Sons Inc	1994			EP 0599444 A	HCAPLUS
Flynn, G	1995			US 5424425 A	HCAPLUS
Flynn, G	1996			US 5491143 A	HCAPLUS
Merrell Dow Pharmaceuti				US 5731306 A	HCAPLUS
Merrell Dow Pharmaceuti	1995			WO 9521839 A	HCAPLUS
Merrell Dow Pharmaceuti	1995			WO 9521854 A	HCAPLUS
The Procter & Gamble Co	1996			WO 9629313 A	HCAPLUS
TourWE, D	1992	2	1305	BIOORGANIC & MEDICIN	HCAPLUS

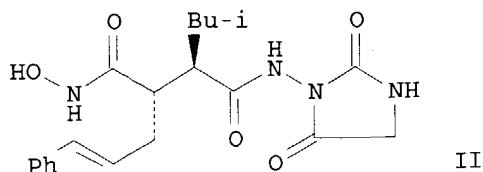
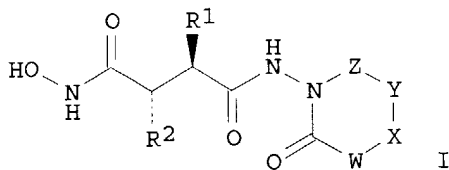
L21 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:421113 HCAPLUS

DOCUMENT NUMBER: 133:58802

TITLE: Preparation of hydroxycarbamoylalkylcarboxylic acid
azacyclic hydrazides as TNF- α inhibitors
INVENTOR(S): Broadhurst, Michael John; Johnson, William Henry;
Walter, Daryl Simon
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035885	A1	20000622	WO 1999-EP9423	19991202
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2353924	AA	20000622	CA 1999-2353924	19991202
BR 9916005	A	20010904	BR 1999-16005	19991202
EP 1137640	A1	20011004	EP 1999-965432	19991202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101644	T2	20011121	TR 2001-200101644	19991202
AU 765729	B2	20030925	AU 2000-20950	19991202
CN 1132819	B	20031231	CN 1999-814323	19991202
US 6281363	B1	20010828	US 1999-457798	19991209
ZA 2001004670	A	20020909	ZA 2001-4670	20010607
PRIORITY APPLN. INFO.:			GB 1998-27408	A 19981211
			GB 1999-25211	A 19991025
			WO 1999-EP9423	W 19991202
OTHER SOURCE(S):			MARPAT 133:58802	
GI				



AB The title hydrazine derivs. (I) [wherein V = a spacer group; W = O, S, CO,

NR5, (CR3R4)m, or forms a fused ring; X and Y = independently CO, NR5, (CH2)n, or forms a fused ring; Z = CO, CS, SO2, or CH2; R1 = (cyclo)alkyl, alkenyl, cycloalkylalkyl, or aryl(alkyl); R2 = (cyclo)alkyl, alkenyl, cycloalkylalkyl, V-aryl, V-heterocyclyl or (CH2)q-CH=CR8R9; R3, R4, and R5 = independently H, (un)substituted, (cyclo)alkyl, alkenyl, cycloalkylalkyl, aryl(alkyl), heterocyclyl(alkyl), or form a fused ring; R8 and R9 together = alkylene in which a CH2 is optionally replaced by a heteroatom; m = 0 or 1; n = 0-2; q = 1 or 2] and their pharmaceutically acceptable salts were prepared For example, II was formed in a 9-step sequence involving (1-3) preparation of (E)-2(R)-[1(S)-(tert-butoxycarbonyl)-4-phenyl-3-butenyl]-4-methylvalerohydrazide, (4) addition of N-(9-fluorenylmethyloxycarbonyl)glycine, (5) N-deprotection, (6) cycloaddn. with phosgene, (7) deesterification, (8) addition of O-(tetrahydro-2H-pyran-2-yl)hydroxylamine, and (9) O-deprotection. Eighteen invention compds. tested for inhibition of bacterial lipopolysaccharide-induced release of tumor necrosis factor alpha (TNF- α) in THP1 cells displayed IC50 of 147-620 nM. In contrast to structurally related hydroxamic acid derivs., I showed only weak inhibitory activity against the matrix metalloproteinase (MMP) family of enzymes, such as collagenases, stromelysins, and gelatinases (no data). I are useful as medicaments, especially in the treatment of

inflammatory

and autoimmune diseases, osteoarthritis, respiratory diseases, tumors, cachexia, cardiovascular diseases, fever, hemorrhage and sepsis.

ED Entered STN: 23 Jun 2000

IC ICM C07D233-80

ICS A61K031-395; C07D239-54; C07D285-18; C07D495-04; C07D233-34; C07D251-34; C07D249-12; C07D241-08; C07D235-02; C07D233-84; C07D471-10; C07D239-96; C07D401-06; C07D233-96; C07D285-10; C07D487-04; C07D495-04; C07D333-00; C07D239-00

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT Respiratory tract

(disease, treatment; preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (**thio**)phosgene with carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

IT Anti-inflammatory agents

Antiarthritics

Antipyretics

Antitumor agents

Cardiovascular agents

(preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (**thio**)phosgene with carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

IT Hydrazides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (**thio**)phosgene with carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

IT Tumor necrosis factors

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)

(preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (**thio**)phosgene with

carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

IT Autoimmune disease

Cachexia

Hemorrhage

Sepsis

(treatment; preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (**thio**)phosgene with carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

IT	277303-69-2P	277303-71-6P	277303-73-8P	277303-74-9P	277303-76-1P
	277303-77-2P	277303-78-3P	277303-79-4P	277303-80-7P	277303-81-8P
	277303-82-9P	277303-83-0P	277303-84-1P	277303-85-2P	277303-86-3P
	277303-87-4P	277303-88-5P	277303-89-6P	277303-90-9P	277303-91-0P
	277303-92-1P	277303-93-2P	277303-94-3P	277303-95-4P	277303-97-6P
	277303-98-7P	277303-99-8P	277304-00-4P	277304-01-5P	277304-02-6P
	277304-03-7P	277304-04-8P	277304-05-9P	277304-06-0P	277304-07-1P
	277304-08-2P	277304-09-3P	277304-11-7P	277304-13-9P	277304-15-1P
	277304-17-3P	277304-19-5P	277304-21-9P	277304-23-1P	277304-24-2P
	277304-26-4P	277304-27-5P	277304-28-6P	277304-29-7P	277304-30-0P
	277304-31-1P	277304-32-2P	277304-33-3P	277304-34-4P	277304-35-5P
	277304-36-6P	277304-37-7P	277304-38-8P	277304-39-9P	277304-40-2P
	277304-41-3P	277304-42-4P	277304-43-5P	277304-44-6P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (**thio**)phosgene with carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

IT	98-09-9, Benzenesulfonyl chloride	100-63-0, Phenylhydrazine	501-53-1, Benzyl chloroformate	555-96-4, Benzylhydrazine	622-33-3, O-Benzylhydroxylamine	1138-80-3, N-(Benzyloxycarbonyl)glycine	1793-07-3, 2-Methoxycarbonylphenyl isocyanate	2949-22-6, Ethyl isocyanatoacetate	3339-73-9, 3-Phthalimidopropionic acid	4392-24-9, Cinnamyl bromide	4403-36-5, 2-Phthalimidoethanesulfonyl chloride	5331-43-1, Benzyl carbazate	6436-90-4, N-Benzyl glycine ethyl ester	6723-30-4, O-(Tetrahydro-2H-pyran-2-yl)hydroxylamine	14667-47-1, Methyl 2-aminonicotinate	17335-90-9, 2,6-Dioxo-4-morpholinecarboxylic acid benzyl ester	21055-37-8, Methyl 2-isothiocyanoacetate	22288-78-4, Methyl 3-aminothiophene-2-carboxylate	29022-11-5, N-(9-Fluorenylmethoxycarbonyl)glycine	30293-85-7, 30293-86-8, 39570-63-3	40203-94-9, 40339-69-3	62402-24-8, N-(2-Pyridylmethyl)glycine ethyl ester	93778-88-2, 106366-62-5, Ethyl 1-isocyanato-1-cyclobutanecarboxylate	112245-04-2, 114877-91-7, 120219-17-2	122246-58-6, 123639-56-5	128326-91-0, 128421-86-3, N-[2-[[[(1,1-Dimethylethoxy)carbonyl]amino]ethyl]glycine methyl ester	129799-08-2, 144876-60-8, 2-(Trimethylsilyl)ethyl 1-isocyanato-1-cyclohexanecarboxylate	145080-94-0, 145080-95-1	186969-63-1, 206761-74-2	253795-93-6, 277305-65-4	277305-66-5, 277305-67-6, 277305-68-7	277305-69-8, 277305-70-1	277305-71-2, 277305-72-3
----	-----------------------------------	---------------------------	--------------------------------	---------------------------	---------------------------------	---	---	------------------------------------	--	-----------------------------	---	-----------------------------	---	--	--------------------------------------	--	--	---	---	------------------------------------	------------------------	--	--	---------------------------------------	--------------------------	---	---	--------------------------	--------------------------	--------------------------	---------------------------------------	--------------------------	--------------------------

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (**thio**)phosgene with carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

IT	189323-10-2P	219614-24-1P	219614-25-2P	219614-39-8P	219615-70-0P
	253795-36-7P	253796-29-1P	277304-45-7P	277304-46-8P	277304-47-9P
	277304-48-0P	277304-49-1P	277304-51-5P	277304-52-6P	277304-53-7P
	277304-54-8P	277304-55-9P	277304-56-0P	277304-57-1P	277304-58-2P

277304-59-3P	277304-60-6P	277304-61-7P	277304-62-8P	277304-63-9P
277304-64-0P	277304-65-1P	277304-66-2P	277304-67-3P	277304-68-4P
277304-69-5P	277304-70-8P	277304-71-9P	277304-72-0P	277304-73-1P
277304-74-2P	277304-75-3P	277304-76-4P	277304-77-5P	277304-78-6P
277304-79-7P	277304-80-0P	277304-81-1P	277304-82-2P	277304-83-3P
277304-84-4P	277304-85-5P	277304-86-6P	277304-87-7P	277304-88-8P
277304-89-9P	277304-90-2P	277304-91-3P	277304-92-4P	277304-93-5P
277304-94-6P	277304-95-7P	277304-96-8P	277304-97-9P	277304-98-0P
277304-99-1P	277305-00-7P	277305-02-9P	277305-03-0P	277305-04-1P
277305-05-2P	277305-06-3P	277305-07-4P	277305-08-5P	277305-09-6P
277305-10-9P	277305-11-0P	277305-12-1P	277305-13-2P	277305-14-3P
277305-15-4P	277305-16-5P	277305-17-6P	277305-18-7P	277305-20-1P
277305-22-3P	277305-24-5P	277305-26-7P	277305-28-9P	277305-29-0P
277305-30-3P	277305-31-4P	277305-32-5P	277305-34-7P	277305-35-8P
277305-36-9P	277305-37-0P	277305-38-1P	277305-39-2P	277305-40-5P
277305-41-6P	277305-42-7P	277305-43-8P	277305-44-9P	277305-45-0P
277305-46-1P	277305-47-2P	277305-48-3P	277305-49-4P	277305-50-7P
277305-51-8P	277305-52-9P	277305-53-0P	277305-54-1P	277305-55-2P
277305-56-3P	277305-57-4P	277305-58-5P	277305-59-6P	277305-60-9P
277305-61-0P	277305-62-1P	277305-63-2P	277305-64-3P	

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of hydroxycarbamoylalkylcarboxylic acid azacyclic hydrazides as TNF- α inhibitors by cycloaddn. of (thio)phosgene with carboxyalkylcarboxylic acid hydrazides and subsequent treatment with hydroxylamines)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
F Hoffmann-La Roche Ag	1995			WO 9533709 A	HCAPLUS
F Hoffmann-La Roche Ag	1999			DE 19829229 A	HCAPLUS

L21 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:210116 HCAPLUS

DOCUMENT NUMBER: 132:251070

TITLE: Preparation and utilization of novel thiol derivatives

INVENTOR(S): Yamashita, T Takizawa, Masayuki;
Yoshimura, F

PATENT ASSIGNEE(S): Takeda Chemi ipan

SOURCE: PCT Int. App
CODEN: PIXXI

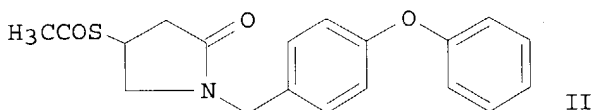
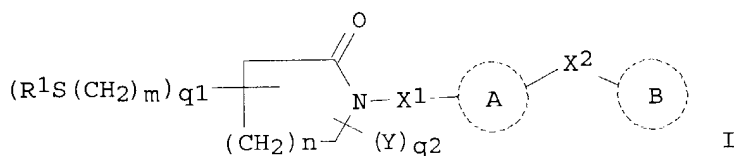
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017162	A1	20000330	WO 1999-JP5103	19990920
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2344412	AA	20000330	CA 1999-2344412	19990920

AU 9956537	A1	20000410	AU 1999-56537	19990920
JP 2000159747	A2	20000613	JP 1999-266295	19990920
EP 1132379	A1	20010912	EP 1999-943412	19990920
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6420415	B1	20020716	US 2001-787623	20010320
US 2003078253	A1	20030424	US 2002-161289	20020603
US 6699881	B2	20040302		
US 2004157894	A1	20040812	US 2004-757325	20040113
PRIORITY APPLN. INFO.:			JP 1998-266037	A 19980921
			WO 1999-JP5103	W 19990920
			US 2001-787623	A3 20010320
			US 2002-161289	A3 20020603
OTHER SOURCE(S):			MARPAT 132:251070	
GI				



AB Title compds [I; wherein the rings A and B represent each an optionally substituted homocycle or heterocycle, etc.; R1s are the same or different and each represents hydrogen, optionally substituted hydrocarbyl, acyl, etc.; X1 represents a bond, optionally substituted divalent aliphatic hydrocarbyl, etc.; X2 represents a bond, optionally substituted divalent aliphatic hydrocarbyl, O, etc.; Ys are the same or different and each represents hydrogen, optionally substituted hydrocarbyl, oxo, etc.; m is 0 or 1; n is an integer of 1 to 3; q1 is an integer of 1 to 2n+4; and q2 is an integer of 0 to 2n+3, provided that q1+q2 is 2n+4], stereoisomers, and salts thereof are prepared and tested as matrix **metalloprotease** inhibitors and are useful as drugs. The title compound (R)-II was prepared and tested.

ED Entered STN: 31 Mar 2000

IC ICM C07D207-26

ICS C07D207-40; C07D211-88; C07D405-12; C07D403-12; C07D401-12;
C07D409-12; A61K031-40; A61K031-44; A61K031-445; A61K031-505;
A61K031-535; C07M007-00

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

ST phenoxybenzylpyrrolidinedione prepn matrix **metalloprotease**
inhibitor; phenoxybenzyl **mercaptopyrrolidinedione** prepn matrix
metalloprotease inhibitor

IT Arthritis
 (acute; preparation of **thiol** derivs. as drug)

IT Gingiva
 (disease; preparation of **thiol** derivs. as drug)

IT Eye, disease
 (keratopathy, ulcer; preparation of **thiol** derivs. as drug)

IT Antiarthritics
 Antitumor agents
 (preparation of **thiol** derivs. as drug)

IT Osteoporosis
 (therapeutic agents; preparation of **thiol** derivs. as drug)

IT 262286-66-8P 262286-72-6P 262286-75-9P 262286-80-6P 262286-82-8P
 262286-86-2P 262286-89-5P 262286-90-8P 262286-92-0P 262286-95-3P
 262286-97-5P 262286-99-7P 262287-01-4P 262287-03-6P 262287-05-8P
 262287-11-6P 262287-23-0P 262287-25-2P 262287-37-6P 262287-43-4P
 262287-54-7P 262287-60-5P 262287-73-0P 262287-75-2P 262287-77-4P
 262287-81-0P 262287-85-4P 262287-88-7P 262287-90-1P 262287-93-4P
 262287-95-6P 262287-97-8P 262287-99-0P 262288-03-9P 262288-05-1P
 262288-07-3P 262288-11-9P 262288-13-1P 262288-16-4P 262288-18-6P
 262288-20-0P 262288-22-2P 262288-25-5P 262288-26-6P 262288-28-8P
 262288-30-2P 262288-32-4P 262288-34-6P 262288-36-8P 262288-38-0P
 262288-40-4P 262288-42-6P 262288-46-0P 262288-48-2P 262288-50-6P
 262288-53-9P 262288-59-5P 262864-44-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of **thiol** derivs. as matrix metalloprotease inhibitors)

IT 262286-67-9P 262286-68-0P 262286-69-1P 262286-70-4P 262286-71-5P
 262286-73-7P 262286-74-8P 262286-76-0P 262286-77-1P 262286-78-2P
 262286-79-3P 262286-81-7P 262286-83-9P 262286-84-0P 262286-85-1P
 262286-87-3P 262286-88-4P 262286-91-9P 262286-93-1P 262286-94-2P
 262286-96-4P 262286-98-6P 262287-00-3P 262287-02-5P 262287-04-7P
 262287-06-9P 262287-07-0P 262287-08-1P 262287-09-2P 262287-10-5P
 262287-12-7P 262287-13-8P 262287-14-9P 262287-15-0P 262287-16-1P
 262287-17-2P 262287-18-3P 262287-19-4P 262287-20-7P 262287-21-8P
 262287-22-9P 262287-24-1P 262287-26-3P 262287-27-4P 262287-28-5P
 262287-29-6P 262287-30-9P 262287-31-0P 262287-32-1P 262287-33-2P
 262287-34-3P 262287-35-4P 262287-36-5P 262287-38-7P 262287-39-8P
 262287-40-1P 262287-41-2P 262287-42-3P 262287-44-5P 262287-45-6P
 262287-46-7P 262287-47-8P 262287-48-9P 262287-49-0P 262287-50-3P
 262287-51-4P 262287-52-5P 262287-53-6P 262287-55-8P 262287-56-9P
 262287-57-0P 262287-58-1P 262287-59-2P 262287-61-6P 262287-62-7P
 262287-63-8P 262287-64-9P 262287-65-0P 262287-66-1P 262287-67-2P
 262287-68-3P 262287-69-4P 262287-70-7P 262287-71-8P 262287-72-9P
 262287-74-1P 262287-76-3P 262287-78-5P 262287-79-6P 262287-80-9P
 262287-82-1P 262287-83-2P 262287-84-3P 262287-86-5P 262287-87-6P
 262287-89-8P 262287-91-2P 262287-92-3P 262287-94-5P 262287-96-7P
 262287-98-9P 262288-00-6P 262288-01-7P 262288-02-8P 262288-04-0P
 262288-06-2P 262288-08-4P 262288-09-5P 262288-10-8P 262288-12-0P
 262288-14-2P 262288-15-3P 262288-17-5P 262288-19-7P 262288-21-1P
 262288-23-3P 262288-24-4P 262288-27-7P 262288-29-9P 262288-31-3P
 262288-33-5P 262288-35-7P 262288-37-9P 262288-39-1P 262288-41-5P
 262288-43-7P 262288-44-8P 262288-45-9P 262288-47-1P 262288-49-3P
 262288-51-7P 262288-52-8P 262288-54-0P 262288-55-1P 262288-56-2P
 262288-57-3P 262288-58-4P 262288-60-8P 262863-82-1P 262863-83-2P
 262864-42-6P 262864-43-7P 262864-45-9P 262864-47-1P 262864-48-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **thiol** derivs. as matrix **metalloprotease**
inhibitors)

IT 141907-41-7, Matrix **metalloprotease**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)

(preparation of **thiol** derivs. as matrix **metalloprotease**
inhibitors)

IT 67-36-7, 4-Phenoxybenzaldehyde 98-91-9, **Thiobenzoic acid**
100-52-7, Benzaldehyde, reactions 103-71-9, Phenylisocyanate, reactions
106-48-9 110-78-1, Propylisocyanate 132-64-9, Dibenzofuran 150-30-1,
Phenylalanine 328-39-2, Leucine 371-41-5, 4-Fluorophenol 459-57-4
533-31-3, 1,3-Benzodioxol-5-ol 589-15-1, p-Bromobenzyl bromide
590-92-1, 3-Bromopropionic acid 611-95-0, 4-Benzoylbenzoic acid
623-00-7 623-05-2, 4-Hydroxybenzyl alcohol 623-33-6, Glycine ethyl
ester hydrochloride 924-49-2, 4-Amino-3-hydroxybutyric acid 1192-30-9,
Tetrahydrofurfuryl bromide 1208-87-3 2417-72-3, Methyl
4-(bromomethyl)-benzoate 2491-20-5, L-Alanine methyl ester hydrochloride
3173-56-6, Benzyl isocyanate 5027-16-7 5332-26-3, N-
(Bromomethyl)phthalimide 5445-44-3 5466-06-8, 3-
Mercaptopropionic acid ethyl ester 5551-11-1,
4-Chloro-2-nitrobenzaldehyde 6667-60-3 6908-41-4, Methyl
4-hydroxymethylbenzoate 6953-60-2, S-**Acetylmercaptosuccinic**
acid anhydride 7144-05-0, 4-Aminomethylpiperidine 16533-72-5,
cis-Epoxy succinic acid 18600-42-5, 4-Nitrobenzylamine hydrochloride
22677-21-0 25747-41-5, 4-Hydroxy-2-pyrrolidone 27019-47-2,
 β -Alanine benzyl ester p-toluenesulfonate 36239-09-5,
Ethyl-3-chloro-3-oxopropionate 39515-51-0, 3-Phenoxybenzaldehyde
40200-69-9 78456-17-4 85319-59-1 95922-54-6 107622-80-0
118468-18-1 169944-04-1 262862-59-9 262862-60-2 262862-61-3
262862-63-5 262862-71-5 262862-75-9 262864-40-4
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of **thiol** derivs. as matrix **metalloprotease**
inhibitors)

IT 836-42-0P, 4-Benzyloxybenzyl chloride 836-43-1P, 4-Benzyloxybenzyl
alcohol 1188-33-6P 1892-57-5P, 1-Ethyl-3-(3-
dimethylaminopropyl)carbodiimide 2215-77-2P, 4-Phenoxybenzoic Acid
3291-46-1P, cis-Epoxy succinic acid diethyl ester 5619-07-8P,
D,L-Phenylalanine methyl ester hydrochloride 6158-54-9P 6322-53-8P,
D,L-Leucine methyl ester hydrochloride 14297-39-3P 22494-53-7P
23450-30-8P, Methyl 4-benzylbenzoate 29021-91-8P, 3-
Dibenzofurancarboxylic acid 34224-29-8P 34905-00-5P 35714-20-6P,
4-Benzylbenzylalcohol 36602-01-4P 42728-62-1P 56651-56-0P
61343-99-5P 68252-20-0P 71666-05-2P 74004-40-3P 80676-35-3P
87179-81-5P 99419-48-4P 111818-34-9P 124397-37-1P, Methyl
4-phenoxy methylbenzoate 129136-15-8P 137736-06-2P 148776-17-4P,
3-Nitro-4-phenoxybenzaldehyde 167091-96-5P 167091-97-6P 169943-89-9P
194017-71-5P 262861-86-9P 262861-91-6P 262861-92-7P 262862-06-6P
262862-07-7P 262862-08-8P 262862-09-9P 262862-16-8P 262862-17-9P
262862-18-0P 262862-19-1P 262862-20-4P 262862-21-5P 262862-22-6P
262862-23-7P 262862-24-8P 262862-25-9P 262862-26-0P 262862-27-1P
262862-28-2P 262862-29-3P 262862-30-6P 262862-33-9P 262862-34-0P
262862-35-1P 262862-50-0P 262862-51-1P 262862-52-2P 262862-53-3P
262862-54-4P 262862-55-5P 262862-62-4P 262862-64-6P 262862-65-7P
262862-66-8P 262862-67-9P 262862-68-0P 262862-69-1P 262862-70-4P
262862-72-6P 262862-73-7P 262862-74-8P 262862-76-0P 262862-77-1P
262862-78-2P 262862-79-3P 262862-80-6P 262862-81-7P 262862-82-8P
262862-83-9P 262862-84-0P 262862-85-1P 262862-86-2P 262862-87-3P
262862-88-4P 262862-91-9P 262862-92-0P 262862-93-1P 262862-94-2P
262862-95-3P 262862-96-4P 262862-97-5P 262862-98-6P 262862-99-7P

262863-84-3P 262863-85-4P 262863-86-5P 262863-87-6P 262863-88-7P
 262863-89-8P 262863-90-1P 262863-91-2P 262863-92-3P 262863-93-4P
 262863-94-5P 262863-95-6P 262863-96-7P 262863-97-8P 262863-98-9P
 262863-99-0P 262864-00-6P 262864-01-7P 262864-02-8P 262864-03-9P
 262864-04-0P 262864-05-1P 262864-06-2P 262864-07-3P 262864-08-4P
 262864-09-5P 262864-10-8P 262864-11-9P 262864-12-0P 262864-13-1P
 262864-14-2P 262864-15-3P 262864-16-4P 262864-17-5P 262864-18-6P
 262864-19-7P 262864-20-0P 262864-21-1P 262864-22-2P 262864-23-3P
 262864-24-4P 262864-25-5P 262864-26-6P 262864-27-7P 262864-28-8P
 262864-29-9P 262864-30-2P 262864-31-3P 262864-32-4P 262864-33-5P
 262864-34-6P 262864-35-7P 262864-36-8P 262864-37-9P 262864-38-0P
 262864-39-1P 262864-41-5P 262864-46-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of **thiol** derivs. as matrix **metalloprotease** inhibitors)

IT 59587-94-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(α -Ph N-tert-butyloxycarbonylglutamate; preparation of **thiol** derivs. as matrix **metalloprotease** inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
F Hoffmann-La Roche Ag				JP 06065196 A	HCAPLUS
F Hoffmann-La Roche Ag				NO 9302117 A	HCAPLUS
F Hoffmann-La Roche Ag				BR 9302273 A	
F Hoffmann-La Roche Ag				FI 9302692 A	
F Hoffmann-La Roche Ag				AU 9339816 A	HCAPLUS
F Hoffmann-La Roche Ag	1993			EP 574758 A1	HCAPLUS
General Electric Compan				GB 1392628 A	HCAPLUS
General Electric Compan				FR 2146253 A1	HCAPLUS
General Electric Compan				DE 2234149 A	HCAPLUS
General Electric Compan				US 3766138 A	HCAPLUS
General Electric Compan				NL 7209825 A	HCAPLUS
General Electric Compan				BE 786120 A1	HCAPLUS
General Electric Compan				IT 962887 A	HCAPLUS
General Electric Compan				CA 982736 A1	HCAPLUS
General Electric Compan	1974			US 3855239 A	HCAPLUS
Thomas, L	1990	29	197	Biopolymers	

L21 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:27824 HCAPLUS

DOCUMENT NUMBER: 130:95560

TITLE: Preparation of barbituric acid derivatives with antimetastatic and antitumor activity

INVENTOR(S): Oliva, Ambrogio; De Cillis, Gianpiero; Grams, Frank; Livi, Valeria; Zimmermann, Gerd; Menta, Ernesto; Krell, Hans-Willi

PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

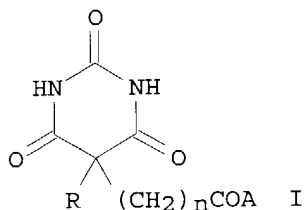
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

WO 9858925 A1 19981230 WO 1998-EP3677 19980618
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9885391 A1 19990104 AU 1998-85391 19980618
AU 746853 B2 20020502
EP 989982 A1 20000405 EP 1998-936361 19980618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
SI, LT, LV, FI, RO
TR 9903148 T2 20000421 TR 1999-9903148 19980618
BR 9810450 A 20000905 BR 1998-10450 19980618
JP 2002504916 T2 20020212 JP 1999-503748 19980618
ZA 9805352 A 19991220 ZA 1998-5352 19980619
MX 9911992 A 20000630 MX 1999-11992 19991217
US 6335332 B1 20020101 US 2000-445461 20000403
PRIORITY APPLN. INFO.: EP 1997-110200 A 19970621
WO 1998-EP3677 W 19980618

OTHER SOURCE(S): MARPAT 130:95560
GI



AB The title compds. [I; R = WV; A = R1, NR2(CH2)_mNR9TR10, etc.; R1 = OH, C1-4 alkoxy, NH2, mono- or di(C1-4 alkyl)amino, (un)substituted phenoxy, benzyloxy, etc.; R9, R10 = H, (un)substituted C1-4 alkyl, Ph, etc.; R9R10NCO may form a 5- or 6-membered lactam ring; T = CO, SO2; V = (un)substituted (un)saturated mono- or bicyclic group optionally containing 1-3 N, O, S; W = bond, C1-8 alkyl, C2-8 alkenyl; n = 1-3] as enantiomers, racemates, diastereoisomers, tautomers or their mixts., and their pharmaceutically acceptable salts, inhibitors of the metzincins useful for the title purpose, were prepared. For example, cyclocondensation of urea with di-Et 2-octylmalonate (preparation by alkylation of di-Et malonate with 1-bromooctane given) gave 5-octylbarbituric acid which was alkylated with BrCH2CO2Et in DMF in the presence of Na2CO3 to give 5-octyl-5-(ethoxycarbonylmethyl)barbituric acid. The latter in vitro inhibited human neutrophil collagenase (MMP-8) with IC50 107 nM and gelatinase 92 kD (MMP-9) with IC50 19.6 nM which gave selectivity (MMP-9/MMP-8) ratio of 0.18-0.2, vs. 0.93 for batimastat as a reference. Approx. 6 I were prepared and approx. 21 I were claimed.

ED Entered STN: 14 Jan 1999
IC ICM C07D401-12
ICS C07D239-62; C07D403-12; A61K031-515
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abbott	1991			EP 0457213 A	HCAPLUS
Adamczyk, M	1997	8	281	Bioconjugate Chemist	HCAPLUS
Al Sharifi, M	1982	34	126	J Pharm Pharmacol	HCAPLUS
Al Sharifi, M	1982		13	THE EFFECT OF ANTIAM	HCAPLUS
Haskins, N	1974	6	181	Adv Mass Spectrom	HCAPLUS
Haskins, N	1975		3	QUALITAT AND QUANTIT	HCAPLUS
Pharm, J	1991	46	293	CHROMIC OXYDATION AN	
Sloan-Kettering Instit	1991			WO 9108191 A	
Talab, A	1992			CHROMIC OXYDATION AN	HCAPLUS
Tecilla, P	1995	51	435	Tetrahedron	HCAPLUS

L21 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:197516 HCAPLUS

DOCUMENT NUMBER: 128:270870

TITLE: Preparation of 3-mercaptoacetyl amino
-1,5-substituted-2-azepinone derivatives as matrix
metalloproteinase inhibitors

INVENTOR(S): Warshawsky, Alan M.; Flynn, Gary A.; Patel, Meena V.;
Beight, Douglas W.; Burkhardt, Joseph P.; Tsay,
Jiu-Tsair; Janusz, Michael J.; Shen, Jian;
Dharanipragada, Ramalinga M.

PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA

SOURCE: PCT Int. Appl., 160 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9812211	A1	19980326	WO 1997-US13738	19970804
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2266759	AA	19980326	CA 1997-2266759	19970804
AU 9738278	A1	19980414	AU 1997-38278	19970804
AU 718055	B2	20000406		
EP 928291	A1	19990714	EP 1997-935308	19970804
EP 928291	B1	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1234039	A	19991103	CN 1997-199024	19970804
BR 9713207	A	20000404	BR 1997-13207	19970804
NZ 334490	A	20000825	NZ 1997-334490	19970804
JP 2001501926	T2	20010213	JP 1998-514658	19970804
AT 229034	E	20021215	AT 1997-935308	19970804
PT 928291	T	20030331	PT 1997-935308	19970804
ES 2184126	T3	20030401	ES 1997-935308	19970804
TW 445262	B	20010711	TW 1997-86113339	19970913

ZA 9708307	A	19980319	ZA 1997-8307	19970915
MX 9902577	A	20000131	MX 1999-2577	19990317
NO 9901316	A	19990518	NO 1999-1316	19990318
KR 2000036246	A	20000626	KR 1999-702336	19990318
HK 1020741	A1	20030502	HK 1999-105993	19991221
PRIORITY APPLN. INFO.:			US 1996-719291	A 19960919
			WO 1997-US13738	W 19970804

OTHER SOURCE(S): MARPAT 128:270870
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to certain novel title compds. I [R1 = C1-6 alkyl, W-(CH2)m, Q-Z-(CH2)m; W = phthalimido; Z = bond, O, NR6, CONR6, NR6CO, NHCONR6, O2CNR6, NHCO2, SO2NR6; Q = H, Y-(CH2)n; Y = H, C6-10 aryl, C3-9 heteroaryl, CO2R6, NR62, morpholino, piperidino, pyrrolidino, isoindolyl; R2 = C1-4 alkyl, (CH2)p-(C3-9) heteroaryl, (CH2)p-Ar1; Ar1 = (un)substituted Ph or naphthyl; R3 = H, C1-6 alkyl, CH2SCH2NHAc, (CH2)p-A, (CH2)m-B, CH2-D-R7; A = C6-10 aryl, C3-9 heteroaryl, cyclohexyl; B = NR72, guanidino, nitroguanidino, CO2R6, CONR6; D = O, S; R4 = H, (CH2)m-S(O)pX1(R6)2; R5 = H, C1-6 alkyl; NR4R5 = piperidino, pyrrolidino, isoindolyl; R6 = H, C1-6 alkyl; R7 = H, C1-4 alkyl, (CH2)p-Ar1; R8 = H, CO2R7, CO(CH2)q-K, S-G; K = nitrogen-containing heterocycle, NR9R10; G = substituted alkyl; R9, R10 = independently C1-4 alkyl, (CH2)p-Ar1; X, X1 = independently CH, N; m = 2-4; n = 0-4; p = 0-2; q = 0-5] as matrix metalloproteinase inhibitors. Pharmaceutical compns. containing said compds. as well as methods of treating various disease states responding to inhibition of matrix metalloproteinase are also claimed herein. Thus, reductive alkylation of H-L-Phe-NHMe.HCl with azido aldehyde II (prepared in 5 steps from 4-phenylcyclohexanone), followed by deesterification and cyclization gave cis azepine III and its corresponding trans isomer in a 4:5 ratio. Reduction of III with 1,3-propanedithiol gave the corresponding amine, which was coupled with 2-bromo-6-phthalimidohexanoic acid to give bromide IV (R = Br). Substitution of IV (R = Br) with p-methoxybenzyl mercaptan followed by deprotection gave title compound IV (R = SH) (MDL 108,180). MDL 108,180 inhibited matrix metalloproteinases MMP-2, MMP-3, and MMP-12 in vitro with Ki = 1.2 nM, 39 nM, and 18 nM, resp.

ED Entered STN: 06 Apr 1998

IC ICM C07K005-078

ICS A61K038-05

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

ST **mercaptoacetylaminoazepinone** prepn matrix metalloproteinase inhibitor; MDL 108180 106540 matrix metalloproteinase inhibitor; azepinone **mercaptoacetylamino** prepn matrix metalloproteinase inhibitor

IT Antiarteriosclerotics

(antiatherosclerotics; preparation of substituted (**mercaptoacetylamino**)azepinone derivs. as matrix metalloproteinase inhibitors)

IT Lung, disease

(chronic obstructive, obstructive; preparation of substituted (**mercaptoacetylamino**)azepinone derivs. as matrix metalloproteinase inhibitors)

IT Eye, disease

Eye, disease

Eye, disease

- (cornea, ulcer; preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT Periodontium
(disease; preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT Gingiva
(gingivitis; preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT Anti-inflammatory agents
Osteoarthritis
Rheumatoid arthritis
(preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT Multiple sclerosis
(therapeutic agents; preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT 79955-99-0, Matrix metalloproteinase-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activated; preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT 205391-09-9P 205391-10-2P 205391-11-3P 205391-12-4P 205391-13-5P
205496-75-9P, MDL 108180 205496-76-0P, MDL 106540
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT 9004-06-2, Matrix metalloproteinase-12 146480-35-5, Matrix metalloproteinase-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT 141907-41-7, Matrix metalloproteinase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT 194934-74-2P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT 60-32-2, 6-Aminocaproic acid 107-11-9, Allylamine 584-93-0, 2-Bromopentanoic acid 589-92-4, 4-Methylcyclohexanone 4894-75-1, 4-Phenylcyclohexanone 6258-60-2, p-Methoxybenzyl mercaptan 13734-34-4 13734-41-3 22509-74-6, N-(Ethoxycarbonyl)phthalimide 90719-32-7, (S)-4-Benzyl-2-oxazolidinone 98541-64-1 205391-40-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
- IT 4443-26-9P 5107-16-4P 131451-47-3P 155387-85-2P 194934-72-0P
194934-75-3P 205391-14-6P 205391-15-7P 205391-16-8P 205391-17-9P
205391-18-0P 205391-19-1P 205391-20-4P 205391-21-5P 205391-22-6P
205391-23-7P 205391-24-8P 205391-25-9P 205391-26-0P 205391-27-1P
205391-28-2P 205391-30-6P 205391-31-7P 205391-32-8P 205391-33-9P
205391-34-0P 205391-35-1P 205391-36-2P 205391-37-3P 205391-38-4P
205391-39-5P 205391-41-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted (**mercaptoacetyl**amino)azepinone derivs.
as matrix metalloproteinase inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Burkholder, E	1993	3	231	BIOORG MED CHEM LETT	
Chiroscience Ltd	1996			WO 9611209 A	HCAPLUS
Kanebo Ltd	1995			JP 07304746 A	HCAPLUS
Procter & Gamble	1996			WO 9629313 A	HCAPLUS
Res Corp Technologies I	1988			WO 8806890 A	HCAPLUS

L21 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:163575 HCAPLUS

DOCUMENT NUMBER: 128:204913

TITLE: Preparation of thiazepinecarboxamide derivatives and
related heterocycles as **metalloprotease**
inhibitors

INVENTOR(S): De, Biswanath; Natchus, Michael George; Pikul,
Stanislaw; Almstead, Neil Gregory; Matthews, Randall
Stryker; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S): Procter & Gamble Company, USA

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808827	A1	19980305	WO 1997-US14551	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2264045	AA	19980305	CA 1997-2264045	19970822
AU 9741529	A1	19980319	AU 1997-41529	19970822
AU 731319	B2	20010329		
EP 925287	A1	19990630	EP 1997-939442	19970822
EP 925287	B1	20030115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1228773	A	19990915	CN 1997-197541	19970822
CN 1232457	A	19991020	CN 1997-198547	19970822
BR 9713185	A	19991103	BR 1997-13185	19970822
JP 2000515166	T2	20001114	JP 1998-511711	19970822
NZ 334252	A	20001124	NZ 1997-334252	19970822
AT 231132	E	20030215	AT 1997-939442	19970822
US 6166005	A	20001226	US 1997-921953	19970826
ZA 9707694	A	19980223	ZA 1997-7694	19970827
ZA 9707695	A	19980223	ZA 1997-7695	19970827
NO 9900839	A	19990428	NO 1999-839	19990222
KR 2000035917	A	20000626	KR 1999-701653	19990227
KR 2000035923	A	20000626	KR 1999-701659	19990227
US 6545038	B1	20030408	US 2000-707212	20001106
US 2003186958	A1	20031002	US 2003-361115	20030206

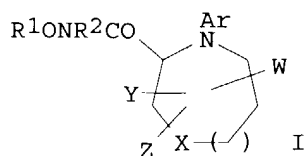
PRIORITY APPLN. INFO.:

US 1996-24764P	P 19960828
WO 1997-US14551	W 19970822
US 1997-921953	A3 19970826
US 2000-707212	A3 20001106

OTHER SOURCE(S):

MARPAT 128:204913

GI



- AB I [R1 = H; R2 = H, alkyl, acyl; Ar = COR3, SO2R4; R3 = alkoxy, alkyl, aryl, etc.; R4 = alkyl, heteroalkyl, aryl, heteroaryl; X = CH2, O, S, SO, SO2, NR5; R5 = H, alkyl, etc.; W = H, alkyl, alkylene or arylene or heteroarylene bridge between two carbons; Y = H, OH, amino, etc.; Z = -, H, spiro moiety, oxo; n = 1-3], inhibitors of **metalloproteases** (no data), were prepared. E.g., N-hydroxy-2,2-dimethyl-S,S-dioxo-4-[(4-methoxyphenyl)sulfonyl]thiazepine-3(S)-carboxamide was prepared using D-penicillamine and 4-methoxybenzenesulfonyl chloride as starting materials.
- ED Entered STN: 19 Mar 1998
- IC ICM C07D243-08
ICS C07D267-10; C07D281-04; C07D281-18; A61K031-53; A61K031-54
- CC 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27, 63
- ST thiazepinecarboxamide sulfonyl prepn **metalloprotease** inhibitor
- IT 204129-53-3P 204129-54-4P 204129-55-5P 204129-56-6P 204129-57-7P
204129-58-8P 204129-59-9P 204129-60-2P 204129-61-3P 204129-62-4P
204129-63-5P 204129-64-6P 204129-65-7P 204129-66-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazepinecarboxamide derivs. and related heterocycles as **metalloprotease** inhibitors)
- IT 81669-70-7, **Metalloprotease**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of thiazepinecarboxamide derivs. and related heterocycles as **metalloprotease** inhibitors)
- IT 52-67-5, D-Penicillamine 98-58-8, 4-Bromobenzenesulfonyl chloride
98-68-0, 4-Methoxybenzenesulfonyl chloride 110-93-0 630-19-3,
Trimethylacetaldehyde 1138-56-3, 4-Butoxybenzenesulfonyl chloride
1655-07-8 5259-98-3, 5-Chloro-1-pentanol 70361-61-4, D-
Cysteine methyl ester hydrochloride 113428-57-2 139937-37-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazepinecarboxamide derivs. and related heterocycles as **metalloprotease** inhibitors)
- IT 53067-23-5P 71135-95-0P 150989-18-7P 150989-20-1P 150989-21-2P
151062-55-4P 204129-67-9P 204129-68-0P 204129-69-1P 204129-70-4P
204129-71-5P 204129-72-6P 204129-73-7P 204129-74-8P 204129-75-9P
204129-76-0P 204129-77-1P 204129-78-2P 204129-79-3P 204129-80-6P
204129-81-7P 204129-82-8P 204129-83-9P 204129-84-0P 204129-85-1P
204129-86-2P 204129-87-3P 204129-88-4P 204129-89-5P 204129-90-8P
204129-91-9P 204129-92-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of thiazepinecarboxamide derivs. and related heterocycles as
metalloprotease inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Agouron Pharmaceuticals	1997			WO 9720824 A	HCAPLUS
Ciba-Geigy	1996			WO 9600214 A	HCAPLUS
F Hoffmann-La Roche Ag	1995			WO 9533731 A	HCAPLUS
Robl, J	1994	4	1795	BIOORGANIC & MEDICIN	HCAPLUS
The Procter & Gamble Co	1996			WO 9620918 A	HCAPLUS
The Procter & Gamble Co	1996			WO 9629313 A	HCAPLUS

L21 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:163563 HCAPLUS

DOCUMENT NUMBER: **128:217281**

TITLE: Preparation and formulation of 1-
arylsulfonylpyrrolidine-2-carboxylates as
metalloprotease inhibitors

INVENTOR(S): Natchus, Michael George; De, Biswanath; Pikul,
Stanislaw; Almstead, Neil Gregory; Bookland, Roger
Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S): Procter & Gamble Company, USA

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

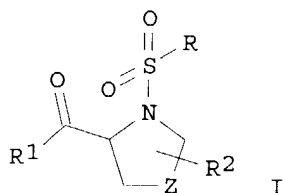
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808815	A1	19980305	WO 1997-US14555	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2263928	AA	19980305	CA 1997-2263928	19970822
AU 9740741	A1	19980319	AU 1997-40741	19970822
AU 741893	B2	20011213		
EP 927161	A1	19990707	EP 1997-938412	19970822
EP 927161	B1	20021016		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1232451	A	19991020	CN 1997-198539	19970822
BR 9713465	A	20000328	BR 1997-13465	19970822
NZ 334256	A	20001124	NZ 1997-334256	19970822
JP 2000516955	T2	20001219	JP 1998-511715	19970822
JP 3541043	B2	20040707		
AT 226193	E	20021115	AT 1997-938412	19970822
PT 927161	T	20031231	PT 1997-938412	19970822
RU 2221782	C2	20040120	RU 1999-106522	19970822
ES 2201318	T3	20040316	ES 1997-938412	19970822
ZA 9707698	A	19980223	ZA 1997-7698	19970827
NO 9900855	A	19990423	NO 1999-855	19990223

KR 2000035922	A	20000626	KR 1999-701658	19990227
HK 1020962	A1	20030808	HK 2000-100036	20000104
JP 2004115531	A2	20040415	JP 2003-384116	20031113
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			JP 1998-511715	A3 19970822
			WO 1997-US14555	W 19970822

OTHER SOURCE(S): MARPAT 128:217281
GI



AB Title compds. [I; R = alkyl, (hetero)aryl, etc.; R1 = OH, alkoxy, NHOH, alkoxyamino; R2 = ≥ 1 of OH, alkyl, alkoxy, (hetero)aryl, etc.; Z = (CH₂)₁₋₃] were prepared as **metalloprotease** inhibitors (no data). Thus, cis-hydroxy-D-proline was N-acylated by 4-(MeO)C₆H₄SO₂Cl and the esterified product amidated by N₂NOK to give (2R,4S)-I [R = C₆H₄(OMe)-4, R1 = NHOH, R2 = H, Z = CH(OH)].

ED Entered STN: 19 Mar 1998

IC ICM C07D207-48
ICS A61K031-40; C07D417-04; C07D403-04; C07D401-04; C07D403-12; C07D401-12; C07D409-14; C07D413-14; C07D405-12

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 34, 63

ST arylsulfonylpyrrolidinecarboxylate prepn **metalloprotease** inhibitor

IT Cachexia
Musculoskeletal diseases
(treatment; preparation and formulation of 1-arylsulfonylpyrrolidine-2-carboxylates as **metalloprotease** inhibitors)

IT 81669-70-7, **Metalloprotease**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; preparation and formulation of 1-arylsulfonylpyrrolidine-2-carboxylates as **metalloprotease** inhibitors)

IT 204071-36-3P 204071-38-5P 204071-40-9P 204071-42-1P 204071-43-2P
204071-44-3P 204071-45-4P 204071-46-5P 204071-47-6P 204071-48-7P
204071-49-8P 204071-50-1P 204071-51-2P 204071-52-3P 204071-53-4P
204071-54-5P 204071-55-6P 204071-56-7P 204071-57-8P 204071-58-9P
204071-59-0P 204071-60-3P 204071-61-4P 204071-62-5P 204071-63-6P
204071-64-7P 204071-65-8P 204071-66-9P 204071-67-0P 204071-68-1P
204071-69-2P 204071-70-5P 204071-71-6P 204071-72-7P 204071-73-8P
204071-74-9P 204071-75-0P 204071-76-1P 204071-77-2P 204071-78-3P
204071-79-4P 204071-80-7P 204071-81-8P 204071-82-9P 204071-83-0P
204071-84-1P 204071-85-2P 204071-86-3P 204071-87-4P 204071-88-5P
204071-89-6P 204071-90-9P 204071-91-0P 204071-92-1P 204071-93-2P
204071-94-3P 204071-95-4P 204071-96-5P 204071-97-6P 204071-98-7P
204071-99-8P 204072-00-4P 204072-01-5P 204072-02-6P 204072-03-7P
204072-04-8P 204072-05-9P 204072-06-0P 204072-07-1P 204072-08-2P
204072-09-3P 204072-10-6P 204072-11-7P 204072-12-8P 204072-14-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of 1-arylsulfonylpyrrolidine-2-carboxylates as **metalloprotease** inhibitors)

IT 60-56-0, 2-Mercapto-1-methylimidazole 65-85-0, Benzoic acid, reactions 77-71-4, 5,5-Dimethylhydantoin 98-58-8, 4-Bromobenzenesulfonyl chloride 98-68-0, 4-Methoxybenzenesulfonyl chloride 100-39-0, Benzyl bromide 100-58-3, Phenylmagnesium bromide 101-18-8, 3-Hydroxydiphenylamine 103-16-2, 4-Benzyloxyphenol 108-95-2, Phenol, reactions 108-98-5, **Thiophenol**, reactions 109-00-2, 3-Hydroxypyridine 111-26-2, 1-Hexanamine 111-30-8, Glutaric dialdehyde 122-78-1, Phenylacetaldehyde 123-38-6, Propionaldehyde, reactions 142-61-0, Hexanoyl chloride 149-30-4, 2-Mercaptobenzothiazole 500-22-1, 3-Pyridinecarboxaldehyde 616-04-6, 1-Methylhydantoin 696-63-9, 4-Methoxy**Thiophenol** 1138-56-3, 4-Butoxybenzenesulfonyl chloride 1499-56-5 1623-92-3, 4-Phenoxybenzenesulfonyl chloride 1806-26-4, 4-n-Octylphenol 2584-71-6, cis-4-Hydroxy-D-proline 3587-60-8, Benzyl chloromethyl ether 3970-21-6, 2-Methoxyethoxymethyl chloride 5414-19-7, Bis(2-bromoethyl) ether 6482-24-2, 2-Bromoethyl methyl ether 7326-19-4 7617-67-6 14002-51-8, [1,1'-Biphenyl]-4-carbonyl chloride 15570-12-4, 3-Methoxy**Thiophenol** 16271-33-3, 2,4-Dichlorobenzenesulfonyl chloride 18092-54-1, 2-Nitro-4-methoxybenzenesulfonyl chloride 23095-31-0, 3,4-Dimethoxybenzenesulfonyl chloride 40856-73-3 51212-37-4, trans-3-Phenylproline 81102-38-7 100836-85-9 114676-47-0 137049-00-4 139937-37-4, 2-Methyl-4-Bromobenzenesulfonyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and formulation of 1-arylsulfonylpyrrolidine-2-carboxylates as **metalloprotease** inhibitors)

IT 1138-54-1P 57850-07-4P 182937-63-9P 203934-42-3P 203934-63-8P
203994-66-5P 203994-80-3P 203994-82-5P 204072-15-1P 204072-16-2P
204072-17-3P 204072-18-4P 204072-19-5P 204072-20-8P 204072-21-9P
204072-22-0P 204072-23-1P 204072-24-2P 204072-25-3P 204072-26-4P
204072-27-5P 204072-28-6P 204072-29-7P 204072-30-0P 204072-31-1P
204072-32-2P 204072-34-4P 204072-36-6P 204072-37-7P 204072-38-8P
204072-39-9P 204072-40-2P 204072-41-3P 204072-42-4P 204072-43-5P
204072-44-6P 204072-45-7P 204072-46-8P 204072-47-9P 204072-49-1P
204072-50-4P 204072-51-5P 204072-52-6P 204072-53-7P 204072-54-8P
204072-55-9P 204072-56-0P 204072-57-1P 204072-58-2P 204072-59-3P
204072-60-6P 204072-61-7P 204072-62-8P 204072-63-9P 204072-64-0P
204072-65-1P 204072-66-2P 204072-67-3P 204072-68-4P 204072-69-5P
204072-70-8P 204072-71-9P 204072-72-0P 204072-73-1P 204072-74-2P
204072-75-3P 204072-76-4P 204072-77-5P 204072-78-6P 204072-79-7P
204072-80-0P 204072-81-1P 204072-82-2P 204072-83-3P 204072-84-4P
204072-85-5P 204072-86-6P 204072-87-7P 204072-88-8P 204072-89-9P
204072-90-2P 204072-91-3P 204072-92-4P 204072-93-5P 204072-94-6P
204072-95-7P 204072-96-8P 204072-97-9P 204072-98-0P 204072-99-1P
204073-00-7P 204073-01-8P 204073-02-9P 204073-03-0P 204073-04-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and formulation of 1-arylsulfonylpyrrolidine-2-carboxylates as **metalloprotease** inhibitors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Agouron Pharmaceuticals	1997			WO 9720824 A	HCAPLUS
Andreatta, R	1967	20	1493	AUST J CHEM	HCAPLUS
Bristol-Myers Co	1988			WO 8802627 A	HCAPLUS
Ciba-Geigy Ag	1994			EP 0606046 A	HCAPLUS

Edwards, M	1996	28	193	ORG PREP, PROCED INT	
Fournier Industrie	1997			WO 9724349 A	HCAPLUS
Heintzelman, G	1996	61	4594	J ORG CHEM	
Herdeis, C	1992	325	419	ARCH PHARM (WEINHEIM	HCAPLUS
Hudson, C	1968	21	769	AUST J CHEM	HCAPLUS
Kahl, J	1981		1445	LIEBIGS ANN CHEM	HCAPLUS
Ono Pharmaceutical Co	1997			EP 0769498 A	HCAPLUS
Pfizer Inc	1996			WO 9633172 A	HCAPLUS
Sanofi	1997			WO 9725315 A	HCAPLUS

L21 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:112235 HCAPLUS

DOCUMENT NUMBER: 128:192934

TITLE: Preparation of peptide β -sheet mimetics as protease and kinase inhibitors and as inhibitors of transcription factors

INVENTOR(S): Kahn, Michael; Qabar, Maher Nicola; McMillan, Michael Kim; Ogbu, Cyprian Okwara; Eguchi, Masakatsu; Kim, Hwa-ok; Boatman, Patrick Douglas, Jr.; Urban, Jan; et al.

PATENT ASSIGNEE(S): Molecumetics Ltd., USA

SOURCE: PCT Int. Appl., 250 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

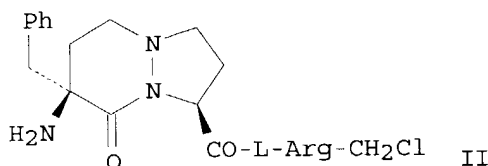
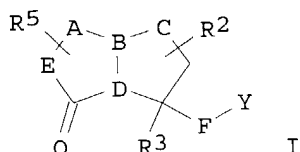
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805333	A1	19980212	WO 1997-US13622	19970805
W: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2262900	AA	19980212	CA 1997-2262900	19970805
AU 9739058	A1	19980225	AU 1997-39058	19970805
AU 732174	B2	20010412		
EP 915700	A1	19990519	EP 1997-936371	19970805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 334227	A	20001027	NZ 1997-334227	19970805
JP 2001524931	T2	20011204	JP 1998-508118	19970805
US 6245764	B1	20010612	US 1998-9665	19980120
US 6117896	A	20000912	US 1998-22934	19980212
NO 9900522	A	19990330	NO 1999-522	19990204
KR 2000029838	A	20000525	KR 1999-700994	19990205
US 6372744	B1	20020416	US 2000-501052	20000209
US 6699869	B1	20040302	US 2000-561107	20000428
US 2003027819	A1	20030206	US 2001-960864	20010921
US 2004230035	A1	20041118	US 2003-745471	20031222
PRIORITY APPLN. INFO.:			US 1996-692420	A 19960805
			US 1996-725073	A 19961002
			US 1997-797915	A 19970210
			US 1997-47067P	P 19970519
			US 1995-410518	B2 19950324

US 1995-549006	B2 19951027
US 1996-624690	B2 19960325
WO 1997-US13622	W 19970805
US 1998-9665	A3 19980120
US 1998-22934	A3 19980212
US 2000-501052	A1 20000209
US 2000-561107	A1 20000428

OTHER SOURCE(S): MARPAT 128:192934
GI



AB β -Sheet mimetics I [A = CO, (CH₂)₀₋₄, CO(CH₂)₁₋₃, (CH₂)₁₋₂CO, (CH₂)₁₋₂S; B = N, CH; C = CO, CO(CH₂)₁₋₃, (CH₂)₀₋₃, O, S, O(CH₂)₁₋₂, S(CH₂)₁₋₂; D = N, CR₄; E = CR₁NH₂, NZ, CR₁Z; F = bond, CO; R₁, R₂, R₄, R₅ = independently amino acid side chain or derivative thereof; R₂ = amino acid side chain or derivative thereof, or taken with C forms a fused substituted or unsubstituted homocyclic or heterocyclic ring; R₃ = amino acid side chain or derivative thereof, or taken with C forms a bridging moiety (CH₂)₁₋₂, O, S; Y, Z represent the remainder of the mol., with the proviso that any two adjacent CH groups of the bicyclic ring may form a double bond] and methods relating to the same are disclosed. The β -sheet mimetics have utility as protease and kinase inhibitors, as well as inhibitors of transcription factors. Methods of the invention include administration of a β -sheet mimetic, or use of the same for the manufacture of a medicament for treatment of a variety of conditions associated with the targeted protease, kinase and/or transcription factor. Thus, bicyclic peptide mimic II was prepared in several steps from phenylalanine Me ester, Et acrylate, and a protected arginine chloromethyl ketone derivative II was tested for inhibitory activity against a variety of serine proteases, and showed IC₅₀ = 1.2 nM against thrombin in an in vitro assay.

ED Entered STN: 25 Feb 1998

ICM A61K031-50

ICS A61K031-435; A61K031-415; A61K031-40; A61K038-00

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT **Thioredoxins**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of peptide β -sheet mimetics as protease and kinase inhibitors and as inhibitors of transcription factors)

IT 9001-01-8, Kallikrein 9001-28-9, Factor IX 9013-55-2, Blood-coagulation factor XI 9026-43-1, Serine kinase 9031-44-1, Kinase 37205-61-1, Protease inhibitor 37259-58-8, Serine protease 37353-41-6, **Cysteine** protease 78169-47-8, Aspartic protease 80449-02-1, Tyrosine kinase 81669-70-7, **Metalloprotease** 97501-93-4, Tryptase

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(preparation of peptide β -sheet mimetics as protease and kinase inhibitors and as inhibitors of transcription factors)

IT 55-81-2, p-Methoxyphenethylamine 56-86-0, L-Glutamic acid, reactions

62-53-3, Benzenamine, reactions 64-04-0, Phenethylamine 78-85-3, Methacrolein 95-16-9, Benzothiazole 100-52-7, Benzaldehyde, reactions 140-88-5 156-41-2, p-Chlorophenethylamine 288-47-1, Thiazole 569-51-7, 1,2,3-Benzenetricarboxylic acid 619-44-3, Methyl 4-iodobenzoate 626-99-3, 2,4-Pentadienoic acid 868-59-7, L-Cysteine ethyl ester hydrochloride 922-67-8, Methyl propiolate 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 2696-85-7, 2-Butylaniline 2987-16-8, 3,3-Dimethylbutyraldehyde 3300-51-4 4336-70-3, Cyanomethyltriphenylphosphonium chloride 5418-86-0, Tris(methylthio)methane 5680-86-4 6294-89-9, Methyl hydrazinocarboxylate 7524-50-7, L-Phenylalanine methyl ester hydrochloride 10236-14-3 15988-11-1, 4-Phenylurazole 17102-64-6, Sorbinol 18598-63-5, L-Cysteine methyl ester hydrochloride 20577-61-1, Methyl 2,4-dioxopentanoate 20849-78-9, 4-(2-Chloroethyl)benzoic acid 71989-26-9 73506-81-7, Hexadienal 92136-39-5 102185-38-6 122235-70-5 183442-86-6 183443-14-3 183443-41-6 203453-89-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptide β -sheet mimetics as protease and kinase inhibitors and as inhibitors of transcription factors)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
=====	=====	=====	=====	=====	=====
Molecumetics Ltd	1996			WO 9630035 A	HCAPLUS
Molecumetics Ltd	1996			WO 9630035 A	HCAPLUS
Scola	1997			WO 9705160 A	HCAPLUS
Scola	1997			WO 9705160 A	HCAPLUS

L21 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:720114 HCAPLUS

DOCUMENT NUMBER: 128:13253

TITLE: Fused pyridine N-hydroxy carboxamide derivatives and analogs as inhibitors of metalloproteases, process for their preparation, and pharmaceutical compositions containing them

INVENTOR(S): De Nanteuil, Guillaume; Paladino, Joseph; Remond, Georges; Atassi, Ghanem; Pierre, Alain; Tucker, Gordon; Bonnet, Jacqueline; Sabatini, Massimo

PATENT ASSIGNEE(S): Adir Et Compagnie, Fr.

SOURCE: Eur. Pat. Appl., 31 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

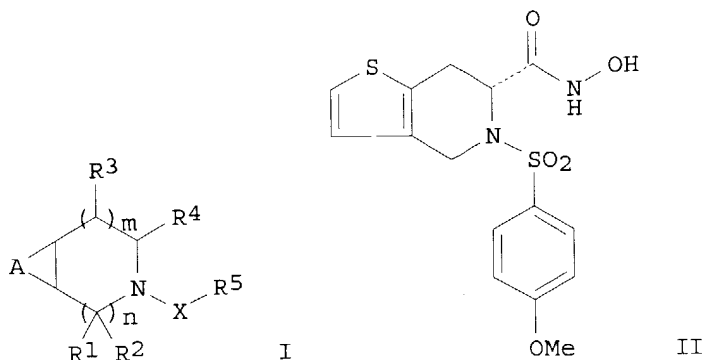
LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
EP 803505	A1	19971029	EP 1997-400913	19970423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
FR 2748026	A1	19971031	FR 1996-5321	19960426
FR 2748026	B1	19980605		
NO 9701862	A	19971027	NO 1997-1862	19970423
CA 2203618	AA	19971026	CA 1997-2203618	19970424
CA 2203618	C	20020528		
AU 9719121	A1	19971030	AU 1997-19121	19970424
AU 713680	B2	19991209		
ZA 9703647	A	19971119	ZA 1997-3647	19970425
CN 1165817	A	19971126	CN 1997-109728	19970425

JP 10059936 A2 19980303 JP 1997-108954 19970425
 US 5866587 A 19990202 US 1997-842982 19970425
 PRIORITY APPLN. INFO.: FR 1996-5321 A 19960426
 OTHER SOURCE(S): CASREACT 128:13253; MARPAT 128:13253
 GI



AB Title compds. I are disclosed [wherein m, n = 0, 1, 2; R1, R2 = H, alkyl, aralkyl, aryl; or R1R2 = O, alkylene; R3 = H, alkyl, OH, alkoxy, or aryl; R4 = CONR6OR6', CSNR6OR6', C(:NH)NR6OR6', CO2R7, NHCONHOH, NHCH2CO2R7, CH(NHR7')CO2R7, CH(CO2R7)2; X = SO2, CO, SO2NH; R5 = alkyl (optionally bearing halo, OH, alkoxy, aryl, or CO2R7), cycloalkyl, aryl, or heterocyclyl; R6, R6' = H or alkyl; R7, R7' = H, alkyl, aralkyl; A = fused aromatic (with provisos) or heterocyclic ring]. I are **metalloprotease** inhibitors, potentially useful for treatment of cancer, rheumatoid arthritis, atherosclerosis, etc. Examples include 30 syntheses of I, 19 prophetic compds., 4 biol. screens for selected compds., and a formulation. For instance, (R)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid hydrochloride underwent a sequence of N-sulfonylation with 4-MeOC6H4SO2Cl, amidation with H2NOCH2CH:CH2.HCl, and Pd-mediated deallylation, to give preferred title compound II. In tests for protection of guinea pig cartilaginous matrix against IL-1 β -induced degradation, II gave 98% protection of collagens and 45% protection of proteoglycans.

ED Entered STN: 14 Nov 1997

IC ICM C07D495-04

ICS C07D471-04; C07D221-10; C07D217-26; C07D209-42; C07D493-04;
 A61K031-435; A61K031-47; A61K031-415; A61K031-40

ICI C07D471-04, C07D221-00, C07D209-00; C07D471-04, C07D221-00, C07D221-00;
 C07D493-04, C07D307-00, C07D221-00; C07D495-04

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 7

ST **metalloprotease** inhibitor thienopyridine carboline
 imidazopyridine isoquinoline; hydroxy carboxamide prepn
metalloprotease inhibitor

IT Antiartherosclerotics
 (antiatherosclerotics; preparation of fused pyridine N-hydroxy carboxamide
 derivs. and analogs as **metalloprotease** inhibitors)

IT Collagens, biological studies
 Proteoglycans, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
 (Miscellaneous); BIOL (Biological study); PROC (Process)

(inhibition of degradation; preparation of fused pyridine N-hydroxy
 carboxamide

- derivs. and analogs as **metalloprotease** inhibitors)
- IT Angiogenesis inhibitors
Antiarthritics
Antitumor agents
(preparation of fused pyridine N-hydroxy carboxamide derivs. and analogs as **metalloprotease** inhibitors)
- IT 158456-85-0P 191327-27-2P 198957-52-7P 198957-53-8P 198957-54-9P
198957-55-0P 198957-56-1P 198957-57-2P 198957-58-3P 198957-59-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate; preparation of fused pyridine N-hydroxy carboxamide derivs.
and analogs as **metalloprotease** inhibitors)
- IT 191326-89-3P 191326-90-6P 191327-21-6P 198957-24-3P 198957-25-4P
198957-26-5P 198957-27-6P 198957-28-7P 198957-29-8P 198957-30-1P
198957-31-2P 198957-32-3P 198957-33-4P 198957-34-5P 198957-35-6P
198957-36-7P 198957-37-8P 198957-38-9P 198957-39-0P 198957-40-3P
198957-41-4P 198957-42-5P 198957-43-6P 198957-44-7P 198957-45-8P
198957-46-9P 198957-47-0P 198957-48-1P 198957-49-2P 198957-50-5P
198957-51-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridine N-hydroxy carboxamide derivs. and analogs as
metalloprotease inhibitors)
- IT 9001-12-1, **MMP**-1 79955-99-0, **MMP**-3 81669-70-7,
Metalloprotease 146480-35-5, **MMP** 2 146480-36-6,
MMP 9
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
(Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of fused pyridine N-hydroxy carboxamide derivs. and analogs as
metalloprotease inhibitors)
- IT 93-11-8, 2-Naphthalenesulfonic acid chloride 98-68-0,
4-Methoxybenzenesulfonic acid chloride 100-07-2, 4-Methoxybenzoic acid
chloride 124-13-0, Octanal 153-94-6, D-Tryptophan 1623-93-4,
4-Phenylbenzenesulfonic acid chloride 42438-90-4 59981-63-4, Spinacine
62561-76-6, β -(2-Thienyl)-D-alanine 72002-54-1 73948-18-2
76985-09-6 78306-92-0 94108-56-2, 4-(Trifluoromethoxy)benzenesulfonic
acid chloride 98667-14-2 103733-65-9, (R)-1,2,3,4-
Tetrahydroisoquinoline-3-carboxylic acid 111139-55-0 198957-60-7
198957-61-8 198957-62-9 198957-63-0 198957-64-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of fused pyridine N-hydroxy carboxamide
derivs. and analogs as **metalloprotease** inhibitors)

L21 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:278955 HCAPLUS

DOCUMENT NUMBER: 126:264355

TITLE: Preparation of N-containing compounds as Fas ligand
solubilization inhibitors

INVENTOR(S): Hirano, Takao; Yagita, Hideo; Okumura, Ko; Hirayama,
Ryoichi; Yamamoto, Minoru; Ebata, Tomohiko; Ohmoto,
Hiroshi; Ikeda, Shoji; Yoshino, Kohichiro

PATENT ASSIGNEE(S): Kanebo, Ltd., Japan

SOURCE: PCT Int. Appl., 123 pp.

CODEN: PIXXD2

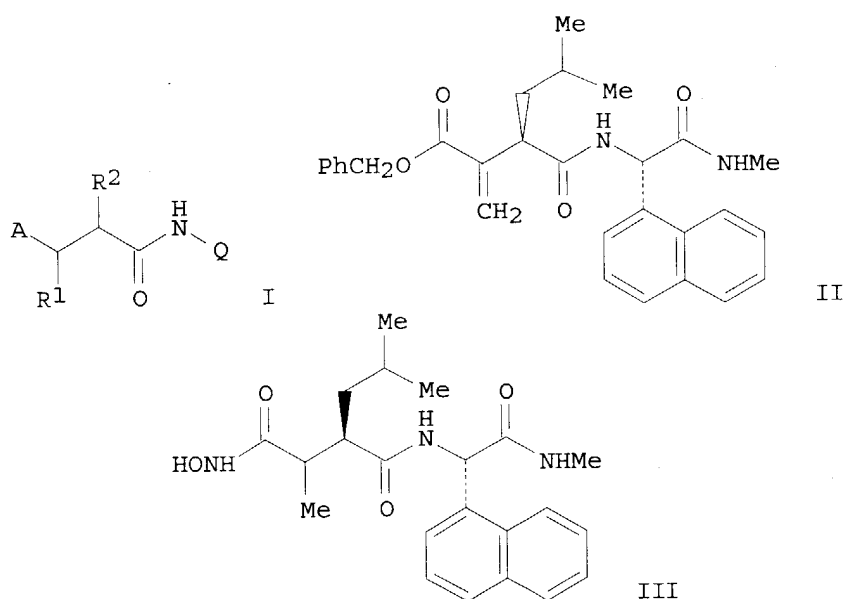
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709066	A1	19970313	WO 1996-JP2492	19960904
W: CA, CN, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 848957	A1	19980624	EP 1996-929510	19960904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 09188631	A2	19970722	JP 1996-257868	19960906
PRIORITY APPLN. INFO.:			JP 1995-256897	19950908
			JP 1995-317136	19951109
			WO 1996-JP2492	19960904
OTHER SOURCE(S):		MARPAT 126:264355		
GI				



AB The title compds. (I; A = N-hydroxyaminocarbonyl, CO₂H, SH, etc.; R¹ = H, NH₂, OH, SH, C1-6 alkoxy or alkyl, etc.; R² = H, C1-6 alkyl or **alkylthio**, C2-6 alkenyl, etc.; R³ = C1-6 alkyl, C2-6 alkenyl, etc.; R⁴ = H, C1-6 alkyl or alkoxy, etc.; R⁵ = H, C1-6 alkyl, etc.; R⁶ = H, OH, C1-6 alkoxy, etc.; R⁷ = H, OH, OMe; n = 5-7) or pharmaceutically acceptable salts thereof are prepared I, having a matrix **metalloprotease** inhibitory activity, are useful as Fas ligand solubilization inhibitors in the prevention or treatment of diseases caused by solubilized Fas ligands such as hepatitis, GVHD, AIDS, and autoimmune diseases. Thus, L-alanine derivative (II) was hydrogenated over Pd/C, reacted with C₆H₄CH₂ONH₂.HCl in the presence of WSC, Et₃N, and hydroxybenzotriazole, and then hydrogenated again over Pd/C to give the title compound (III). III showed 50% Fas ligand secretion inhibitory when tested on mouse p.o.

ED Entered STN: 01 May 1997

IC ICM A61K045-00

ICS A61K031-165; A61K031-47; A61K031-55; C07D487-04; C07C239-18

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 28, 63

ST Fas ligand solubilization inhibitor nitrogen compd; matrix
metalloprotease inhibitor nitrogen compd; hepatitis treatment
 nitrogen compd prepn; GVHD treatment nitrogen compd prepn; AIDS treatment
 nitrogen compd prepn; autoimmune disease treatment nitrogen compd prepn

IT 81669-70-7, **Metalloprotease**
 RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
 (Miscellaneous); BIOL (Biological study); PROC (Process)
 (matrix; preparation of N-containing compds. as Fas ligand solubilization
 inhibitors)

IT 50-00-0, Formaldehyde, reactions 66-99-9, 2-Naphthaldehyde 74-89-5,
 Methylamine, reactions 91-21-4, 1,2,3,4-Tetrahydroisoquinoline
 100-39-0, Benzyl bromide 108-18-9, Diisopropylamine 108-98-5,
Thiophenol, reactions 110-91-8, Morpholine, reactions
 501-53-1, Benzyloxycarbonyl chloride 541-41-3, Ethyl chlorocarbonate
 1821-12-1, 4-Phenylbutyric acid 2270-20-4, 5-Phenylpentanoic acid
 2687-43-6, O-Benzylhydroxylamine hydrochloride 5292-43-3, tert-Butyl
 bromoacetate 18496-54-3, 4-Phenylbutanoyl chloride 41153-30-4
 55447-00-2 56613-80-0 100564-78-1 129213-83-8 133899-27-1
 145963-04-8 155947-71-0 162117-96-6 168158-22-3 170450-78-9
 188729-11-5 188729-12-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of N-containing compds. as Fas ligand solubilization
 inhibitors)

L21 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:731972 HCAPLUS

DOCUMENT NUMBER: **126:8011**

TITLE: Preparation of 3-[(hydroxaminocarbonyl)alkanamido]capr
 olactams and analogs as matrix **metalloprotease**
 inhibitors

INVENTOR(S): De, Biswanath; Cheng, Menyen; Natchus, Michael George;
 Wahl, Christopher Thomas

PATENT ASSIGNEE(S): Procter and Gamble Company, USA

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

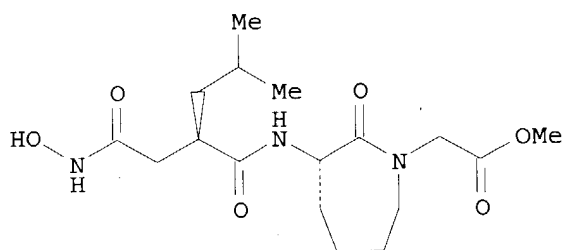
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629313	A1	19960926	WO 1996-US3726	19960319
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
US 5672598	A	19970930	US 1995-407839	19950321
IL 117527	A1	19991222	IL 1996-117527	19960318
CA 2216129	AA	19960926	CA 1996-2216129	19960319
CA 2216129	C	20020820		
AU 9652558	A1	19961008	AU 1996-52558	19960319
AU 711889	B2	19991021		
EP 815084	A1	19980107	EP 1996-908856	19960319
EP 815084	B1	20030827		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1179151	A	19980415	CN 1996-192669	19960319
BR 9607772	A	19980707	BR 1996-7772	19960319

JP 11502523	T2	19990302	JP 1996-528560	19960319
AT 248150	E	20030915	AT 1996-908856	19960319
ZA 9602253	A	19960930	ZA 1996-2253	19960320
NO 9704335	A	19971121	NO 1997-4335	19970919
PRIORITY APPLN. INFO.:			US 1995-407839	A 19950321
			WO 1996-US3726	W 19960319

OTHER SOURCE(S): MARPAT 126:8011

GI



I

- AB HONHCOCHR1CHR2CONR3CHR8CONR4R9 [R1 = H, alkyl, alkoxy, heterocyclyl, etc.; R2 = H, OH, alkyl, heterocyclyl, etc.; R1R2 = alkylene; R3 = H or (cyclo)alkyl; R4 = (cyclo)alkyl, alkoxycarbonyl(alkyl), arylsulfonyl, etc.; R8R9 = (CR2)n, CH:CH, etc.; n = 2-4] were prepared as matrix **metalloprotease** inhibitors (no data). Thus, (S)-caprolactam-3-amine was amidated by (R)-Me3CO2CCH2CH(CH2CHMe2)CO2H and the product N-alkylated by BrCH2CO2Me to give, in 2 addnl. steps, title compound I.
- ED Entered STN: 13 Dec 1996
- IC ICM C07D223-12
ICS C07D211-76; C07D213-75; A61K031-55; A61K031-445; A61K031-44
- CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
- ST alkanamidocaprolactam hydroxaminocarbonyl prepn matrix
metalloprotease inhibitor
- IT 81669-70-7, Metalloproteinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(matrix; mediated diseases; treatment; preparation of 3-
[(hydroxaminocarbonyl)alkanamido]caprolactams and analogs as matrix
metalloprotease inhibitors)
- IT 183665-06-7P 183665-08-9P 183665-09-0P 183665-10-3P 183665-12-5P
183665-14-7P 183665-15-8P 183665-17-0P 183665-18-1P 183665-19-2P
183665-20-5P 183665-21-6P 183665-22-7P 183665-23-8P 183665-26-1P
183665-29-4P 183665-33-0P 183665-34-1P 183665-35-2P 183901-48-6P
183901-49-7P 183901-50-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-[(hydroxaminocarbonyl)alkanamido]caprolactams and analogs as matrix **metalloprotease** inhibitors)
- IT 96-32-2, Methyl bromoacetate 98-59-9, Tosyl chloride 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 109-65-9, 1-Bromobutane 109-73-9, Butylamine, reactions 112-13-0, Decanoyl chloride 622-33-3, O-Benzyl hydroxylamine 2528-61-2, Heptanoyl chloride 3184-13-2, L-Ornithine hydrochloride 5292-43-3, tert-Butyl bromoacetate 5437-45-6, Benzylbromoacetate 6332-56-5, 2-Hydroxy-3-nitropyridine 6482-24-2, 2-BrOmoethyl methyl ether 21568-87-6, (S)-Caprolactam-3-amine 24424-99-5, Di-tert-butyl dicarbonate 90719-32-7, (S)-4-Benzyl-2-

oxazolidinone 112245-04-2 135775-09-6 148415-74-1 148415-75-2
148415-76-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 3-[(hydroxaminocarbonyl)alkanamido]caprolactams and analogs
as matrix **metalloprotease** inhibitors)

IT 34294-79-6P 76944-95-1P 82611-52-7P 92235-39-7P 93961-02-5P
93961-04-7P 153427-69-1P 153427-89-5P 175210-67-0P 183665-36-3P
183665-37-4P 183665-38-5P 183665-39-6P 183665-40-9P 183665-41-0P
183665-42-1P 183665-43-2P 183665-44-3P 183665-45-4P 183665-46-5P
183665-47-6P 183665-48-7P 183665-49-8P 183665-50-1P 183665-51-2P
183665-52-3P 183665-53-4P 183665-54-5P 183665-55-6P 183665-56-7P
183665-57-8P 183665-58-9P 183665-59-0P 183665-60-3P 183665-61-4P
183665-62-5P 183665-63-6P 183665-64-7P 183665-65-8P 183665-66-9P
183665-67-0P 183665-68-1P 183665-70-5P 183665-71-6P 183665-73-8P
183665-76-1P 183665-78-3P 183665-81-8P 183665-83-0P 183665-85-2P
183665-87-4P 183665-88-5P 183665-89-6P 183665-90-9P 183665-91-0P
183665-92-1P 183665-93-2P 183665-94-3P 183665-95-4P 183665-96-5P
183665-97-6P 183665-98-7P 183665-99-8P 183666-00-4P 183666-01-5P
183666-02-6P 183666-03-7P 183666-04-8P 183666-05-9P 183666-06-0P
183666-07-1P 183666-08-2P 183666-09-3P 183666-10-6P 183666-11-7P
183666-12-8P 183901-51-1P 183901-52-2P 183901-53-3P 183901-54-4P
183901-55-5P 183901-56-6P 183901-57-7P 183901-58-8P 183901-59-9P
183901-60-2P 183901-61-3P 183901-62-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of 3-[(hydroxaminocarbonyl)alkanamido]caprolactams and analogs
as matrix **metalloprotease** inhibitors)

L21 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:546363 HCAPLUS

DOCUMENT NUMBER: 125:189378

TITLE: Hydroxamic acid-containing inhibitors of matrix
metalloproteases and their use in
pharmaceuticals

INVENTOR(S): Yelm, Kenneth Edward

PATENT ASSIGNEE(S): Procter and Gamble Company, USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620918	A1	19960711	WO 1995-US16140	19951213
W:	AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5639746	A	19970617	US 1994-366062	19941229
CA 2208679	AA	19960711	CA 1995-2208679	19951213
AU 9644220	A1	19960724	AU 1996-44220	19951213
AU 706409	B2	19990617		
BR 9510175	A	19971014	BR 1995-10175	19951213
EP 800510	A1	19971015	EP 1995-943083	19951213
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE			

CN 1171780	A	19980128	CN 1995-197203	19951213
JP 10512241	T2	19981124	JP 1995-521011	19951213
NO 9703035	A	19970829	NO 1997-3035	19970627
PRIORITY APPLN. INFO.:			US 1994-366062	19941229
			WO 1995-US16140	19951213

OTHER SOURCE(S): MARPAT 125:189378

AB The invention provides hydroxamic acid-containing compds. which are useful as inhibitors of matrix **metalloproteases** and which are effective in treating conditions associated with excess activity of these enzymes. In particular, the present invention relates to a compound having structure HONHCOCHR1NR2COCHR3CHR4COR5 (R1-5 are independently selected from various substituents; or R3 and R4 or R4 and R5 may together comprise a cyclic moiety) or a pharmaceutically-acceptable salt, biohydrolyzable amide or biohydrolyzable ester thereof. In other aspects, the invention is directed to pharmaceutical compns. containing the above compds. and to methods of treating diseases characterized by matrix **metalloprotease** activity using these compds. or the pharmaceutical compns. containing them. Eight of the hydroxamic acid containing inhibitors were synthesized.

ED Entered STN: 13 Sep 1996

IC ICM C07C259-06

ICS A61K031-16

CC 7-3 (Enzymes)

Section cross-reference(s): 21, 63

IT 141907-41-7, Matrix metalloproteinase

RL: MSC (Miscellaneous)

(hydroxamic acid-containing inhibitors of matrix **metalloproteases** and their use in pharmaceuticals)

IT 64-04-0, Phenethylamine 78-81-9, Isobutylamine 112-31-2, Decyl aldehyde 122-78-1, Phenylacetaldehyde 598-21-0, Bromoacetyl bromide 646-07-1, 4-Methylvaleric acid 1438-96-6 2016-57-1, Decylamine 2687-43-6, O-Benzylhydroxylamine hydrochloride 5241-58-7 5292-43-3 7764-95-6 14166-21-3, trans-1,2-Cyclohexanedicarboxylic anhydride 82732-07-8 90719-32-7, (S)-4-Benzyl-2-oxazolidinone

RL: RCT (Reactant); RACT (Reactant or reagent)

(hydroxamic acid-containing inhibitors of matrix **metalloproteases** and their use in pharmaceuticals)

IT 38136-29-7P, 4-Methylvaleroyl chloride 78158-32-4P 112245-04-2P 113543-30-9P 144287-83-2P 180711-88-0P 180711-89-1P 180711-90-4P 180711-91-5P 180711-93-7P 180711-94-8P 180711-96-0P 180711-97-1P 180711-98-2P 180712-00-9P 180712-01-0P 180712-02-1P 180712-04-3P 180712-05-4P 180712-07-6P 180712-08-7P 180712-09-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(hydroxamic acid-containing inhibitors of matrix **metalloproteases** and their use in pharmaceuticals)

IT 180711-92-6P 180711-95-9P 180711-99-3P 180712-03-2P 180712-06-5P 180712-10-1P 180978-86-3P 180978-87-4P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hydroxamic acid-containing inhibitors of matrix **metalloproteases** and their use in pharmaceuticals)

L21 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:95761 HCAPLUS

DOCUMENT NUMBER: 120:95761

TITLE: Use of matrix **metalloprotease** (MMP)

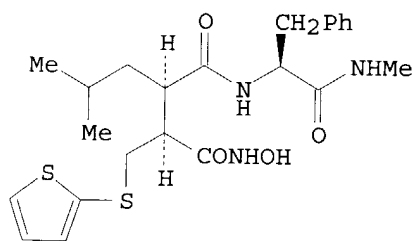
) inhibitors as antitumor agents

INVENTOR(S): Brown, Peter Duncan; Bawden, Lindsay Jayne; Miller, Karen Margrete

PATENT ASSIGNEE(S): British Bio-Technology Ltd., UK

SOURCE: PCT Int. Appl., 48 pp.
 DOCUMENT TYPE: CODEN: PIXXD2
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: English
 PATENT INFORMATION: 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321942	A2	19931111	WO 1993-GB888	19930429
WO 9321942	A3	19940120		
W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, PT, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9342672	A1	19931129	AU 1993-42672	19930429
EP 1002556	A2	20000524	EP 1999-114903	19930429
EP 1002556	A3	20010110		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
ZA 9303089	A	19931123	ZA 1993-3089	19930430
US 5872152	A	19990216	US 1996-686485	19960726
PRIORITY APPLN. INFO.:				
			GB 1992-9513	A 19920501
			GB 1993-5817	A 19930320
			EP 1993-911883	A3 19930429
			WO 1993-GB888	A 19930429
			US 1993-133081	B1 19931202
OTHER SOURCE(S):				
GI MARPAT 120:95761				



AB Various known hydroxamic acid **MMPs** are useful in the preparation of agents for promoting tumor regression and/or inhibiting cancer cell proliferation. Thus, I inhibited proliferation of human melanoma cells in vitro at 3 μ M, and markedly increased the survival time of mice bearing a human ovarian carcinoma xenograft when administered at 40 mg/kg/day i.p.

ED Entered STN: 05 Mar 1994

IC ICM A61K037-02

CC 1-6 (Pharmacology)

IT Psoriasis
 (angiogenesis inhibition in, with matrix **metalloprotease** inhibitors)

IT Blood vessel
 (formation of, matrix **metalloprotease** inhibitors effect on, neoplasm inhibition in relation to)

IT Neoplasm inhibitors
 (matrix **metalloprotease**-inhibiting hydroxamates)

IT Hydroxamic acids
 RL: BIOL (Biological study)
 (matrix **metalloprotease**-inhibiting, neoplasm inhibition by)

IT Diabetes mellitus
(retinopathy in, angiogenesis inhibition in, with matrix
metalloprotease inhibitors)

IT Neoplasm inhibitors
(carcinoma, matrix **metalloprotease**-inhibiting hydroxamates)

IT Kidney, neoplasm
Lung, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(carcinoma, inhibitors, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Uterus, neoplasm
(cervix, carcinoma, inhibitors, matrix **metalloprotease**
-inhibiting hydroxamates)

IT Neoplasm inhibitors
(colon carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Intestine, neoplasm
(colon, carcinoma, inhibitors, matrix **metalloprotease**
-inhibiting hydroxamates)

IT Neoplasm inhibitors
(kidney carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Neoplasm inhibitors
(lung carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Neoplasm inhibitors
(mammary gland carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Neoplasm inhibitors
(melanoma, matrix **metalloprotease**-inhibiting hydroxamates)

IT Neoplasm inhibitors
(metastasis, matrix **metalloprotease**-inhibiting hydroxamates)

IT Mammary gland
Prostate gland
(neoplasm, carcinoma, inhibitors, matrix **metalloprotease**
-inhibiting hydroxamates)

IT Neoplasm inhibitors
(neuroectoderm, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Nervous system
(neuroectoderm, neoplasm, inhibitors, matrix **metalloprotease**
-inhibiting hydroxamates)

IT Neoplasm inhibitors
(ovary carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Neoplasm inhibitors
(pancreas carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Neoplasm inhibitors
(prostate gland carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Eye, disease
(pterygium, angiogenesis inhibition in, with matrix
metalloprotease inhibitors)

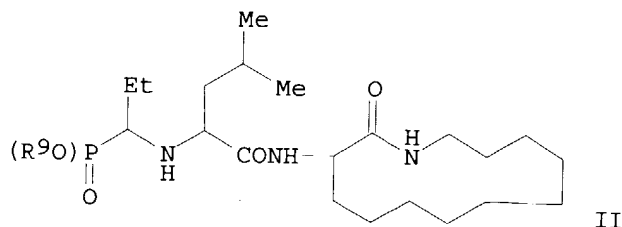
IT Neoplasm inhibitors
(rectum carcinoma, matrix **metalloprotease**-inhibiting
hydroxamates)

IT Intestine, neoplasm

(rectum, carcinoma, inhibitors, matrix **metalloprotease**-inhibiting hydroxamates)
 IT Eye, disease
 (retinopathy, in diabetes mellitus, angiogenesis inhibition in, with matrix **metalloprotease** inhibitors)
 IT Neoplasm inhibitors
 (sarcoma, matrix **metalloprotease**-inhibiting hydroxamates)
 IT Neoplasm inhibitors
 (stomach carcinoma, matrix **metalloprotease**-inhibiting hydroxamates)
 IT Neoplasm inhibitors
 (uterus cervix carcinoma, matrix **metalloprotease**-inhibiting hydroxamates)

L21 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1991:229399 HCAPLUS
 DOCUMENT NUMBER: 114:229399
 TITLE: Preparation of phosphonoalkylpeptides with collagenase inhibiting activity
 INVENTOR(S): Markwell, Roger Edward; Ward, Robert William; Hunter, David James
 PATENT ASSIGNEE(S): Beecham Group PLC, UK
 SOURCE: Eur. Pat. Appl., 29 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 401963	A1	19901212	EP 1990-303851	19900410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2014375	AA	19901013	CA 1990-2014375	19900411
AU 9053158	A1	19901018	AU 1990-53158	19900411
AU 618669	B2	19920102		
ZA 9002775	A	19910626	ZA 1990-2775	19900411
JP 03063294	A2	19910319	JP 1990-96589	19900413
US 5212163	A	19930518	US 1991-758356	19910909
PRIORITY APPLN. INFO.:			GB 1989-8353	A 19890413
			GB 1989-17756	A 19890803
			US 1990-508272	B1 19900411
OTHER SOURCE(S):			MARPAT 114:229399	
GI				



AB HO(RO)P(O)CHR1NHCHR2CONHCHR3CONHR4 [I; R = H, C1-6 alkyl, (substituted) PhCH2; R1 = H, C1-6 alkyl; R2 = C3-6 alkyl; R3 = H, alkyl, CH2Z, CHR8OR7; Z = (substituted) Ph or heteroaryl; R7 = H, alkyl, (substituted) PhCH2; R8

= H, alkyl; R4 = CH₂(CH₂)_nOR₅, CH₂(CH₂)_nO₂CR₆; n = 1-6; R₅, R₆ = H, C₁-6 alkyl; or R₃R₄ = (CH₂)_m; m = 4-12], useful as inhibitors of neutral **metalloproteases** for treatment of arthritic diseases, bone resorption diseases, degradation of connective tissue, etc., are prepared

Thus, condensation of N-[(S)-1-diethoxyphosphinylpropyl]-(R or S)-leucine with (-)-3-aminoazacyclotridecan-2-one in the presence of 1-hydroxybenzotriazole and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide-HCl in CH₂Cl₂ and deprotection of the resulting amide (II; R₉ = Et) with Me₃SiBr in CH₂Cl₂ gave II (R₉ = H) (III). (S,S)-III in vitro showed IC₅₀ = 0.045 μM against human lung fibroblast collagenase.

ED Entered STN: 15 Jun 1991

IC ICM C07K005-06

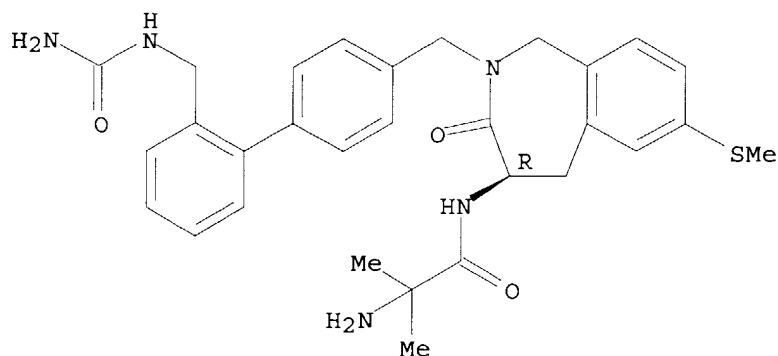
ICS C07F009-38; A61K037-64; A61K031-66

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 7

=>

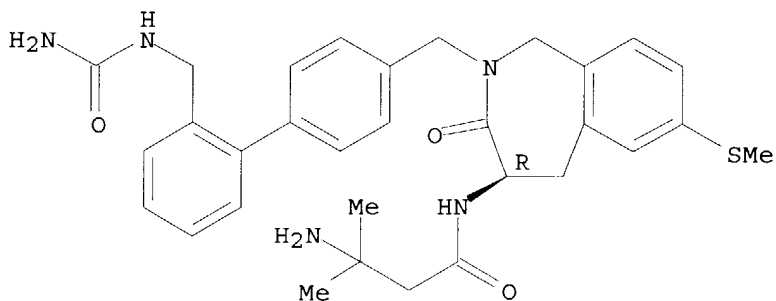
=>



RN 168057-69-0 HCAPLUS

CN Butanamide, 3-amino-N-[2-[[2'-[[[(aminocarbonyl)amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

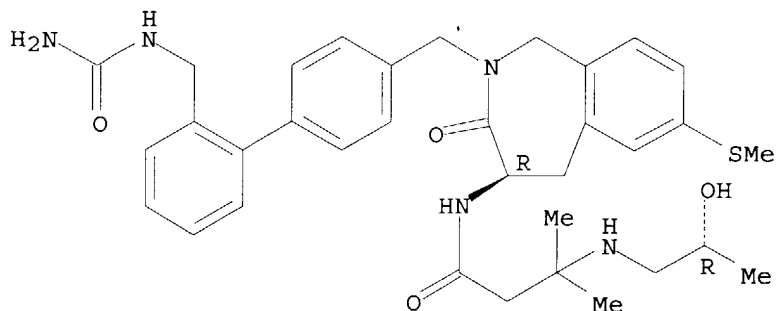
Absolute stereochemistry.



RN 168057-72-5 HCAPLUS

CN Butanamide, N-[2-[[2'-[[[(aminocarbonyl)amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

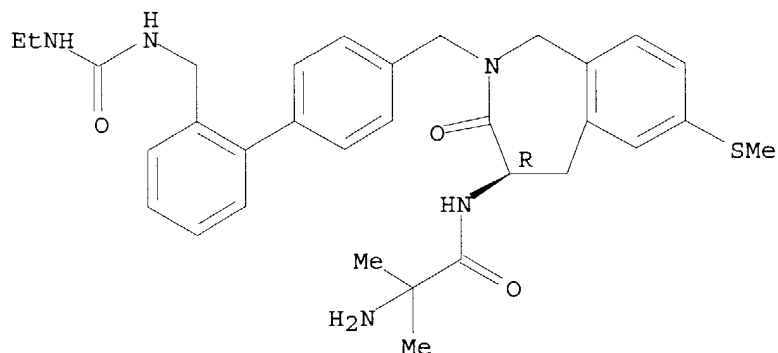
Absolute stereochemistry.



RN 168057-78-1 HCAPLUS

CN Propanamide, 2-amino-N-[2-[[2'-[[[(ethylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

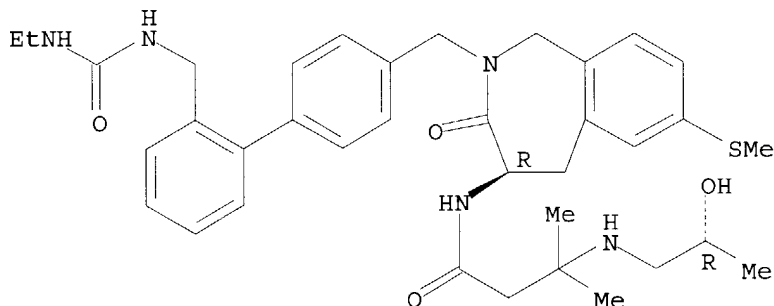
Absolute stereochemistry.



RN 168057-84-9 HCAPLUS

CN Butanamide, N-[2-[[2'-[[[(ethylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

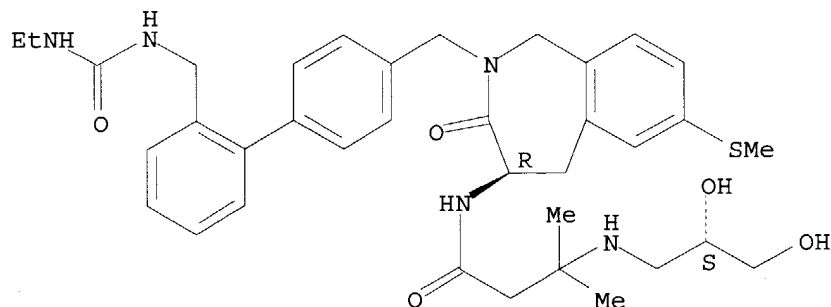
Absolute stereochemistry.



RN 168057-88-3 HCAPLUS

CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-N-[2-[[2'-[[[(ethylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-methyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

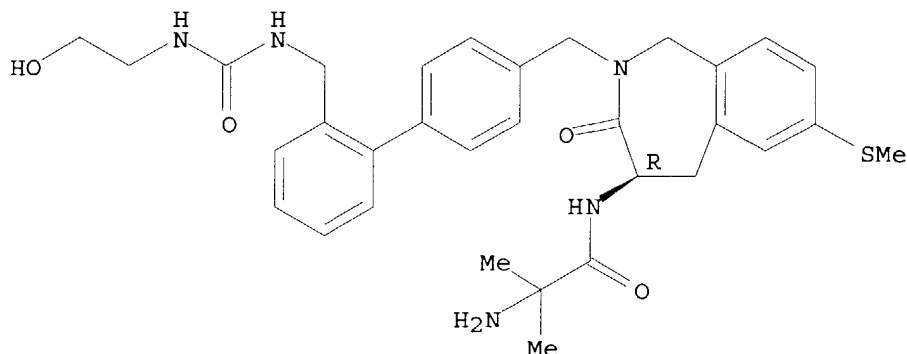
Absolute stereochemistry.



RN 168057-92-9 HCAPLUS

CN Propanamide, 2-amino-2-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

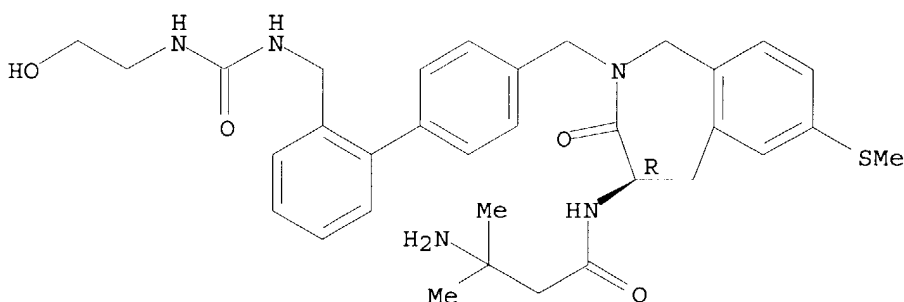
Absolute stereochemistry.



RN 168057-96-3 HCAPLUS

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

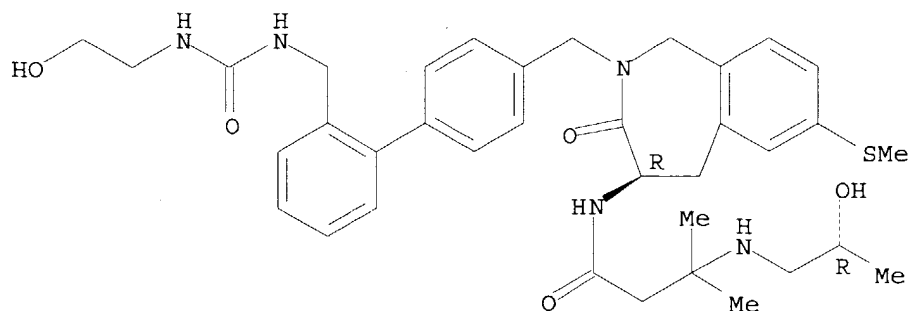
Absolute stereochemistry.



RN 168058-00-2 HCAPLUS

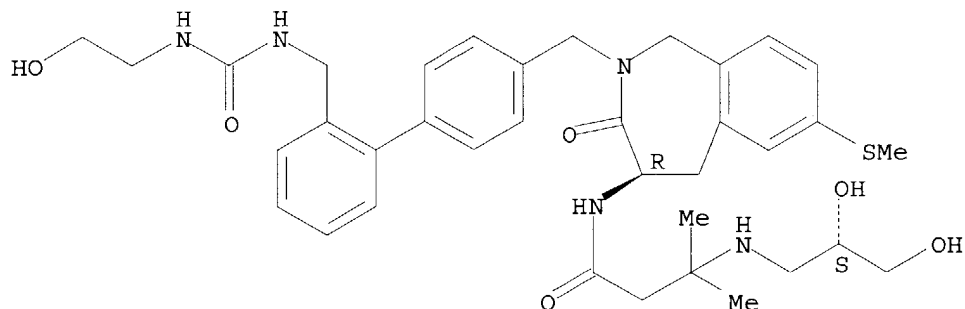
CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168058-04-6 HCAPLUS
 CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, [R-(R*,S*)]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



L52 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:867574 HCAPLUS
 DOCUMENT NUMBER: 123:256544
 ENTRY DATE: Entered STN: 20 Oct 1995
 TITLE: Preparation of N-(oxobenzazepinyl)alkanamides as growth hormone release promoters
 INVENTOR(S): Schoen, William R.; Wyvratt, Matthew J., Jr.; Hodges, Paul J.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: PCT Int. Appl., 134 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: C07D281-10
 SECONDARY: C07D223-16; C07D281-18; C07D223-06; A61K031-55
 CLASSIFICATION: 27-21 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9503290	A1	19950202	WO 1994-US8228	19940720

W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KR, KZ,
LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ,
TT, UA, US, UZ

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5430144	A	19950704	US 1993-97146	19930726
CA 2167507	AA	19950202	CA 1994-2167507	19940720
AU 9474024	A1	19950220	AU 1994-74024	19940720
AU 683081	B2	19971030		
EP 711287	A1	19960515	EP 1995-906200	19940720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09502961	T2	19970325	JP 1994-505304	19940720
ZA 9405462	A	19950303	ZA 1994-5462	19940725

PRIORITY APPLN. INFO.:

US 1993-97146	A	19930726
WO 1994-US8228	W	19940720

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9503290	ICM	C07D281-10
	ICS	C07D223-16; C07D281-18; C07D223-06; A61K031-55
US 5430144	ECLA	C07D403/14; C07D405/12; C07D405/14; C07D417/14

OTHER SOURCE(S): CASREACT 123:256544; MARPAT 123:256544

GRAPHIC IMAGE: For diagram(s), see printed CA Issue.

ABSTRACT:

Title compds. [I; A = (CH₂)_xCR₈R₈₀(CH₂)_y; R = (CH₂)_qZwR₂₀; R₁,R₂ = H, halo, alkyl, Ph, etc.; R₄ = furfuryl, azolyl(alkyl), etc.; R₅ = H, alkyl, Ph, etc.; R₆ = H, alkyl, phenyl(alkyl); R₈,R₈₀ = H, alkyl, Ph, etc.; R₂₀ = (un)substituted Ph; Z = (un)substituted phenylene; n,w = 0 or 1; p,x,y = 0-3; q = 0-4] were prepared as growth hormone release promoters (no data). Thus, title compound II (R₄ = H) was reductively condensed with furfuraldehyde to give II (R₄ = furfuryl).

SUPPL. TERM: oxobenzazepinylalkanamide prepn growth hormone release promoter

INDEX TERM: Antiobesity agents
(preparation of N-(oxobenzazepinyl)alkanamides as growth hormone release promoters)

INDEX TERM: Osteoporosis
(treatment; preparation of N-(oxobenzazepinyl)alkanamides as growth hormone release promoters)

INDEX TERM: Animal metabolism
(disorder, catabolic, nitrogen wasting; treatment; preparation of N-(oxobenzazepinyl)alkanamides as growth hormone release promoters)

INDEX TERM:	169187-15-9P	169187-16-0P	169187-18-2P	169187-20-6P
	169187-21-7P	169187-22-8P	169187-23-9P	169187-24-0P
	169187-25-1P	169187-26-2P	169187-27-3P	169187-28-4P
	169187-29-5P	169187-30-8P	169187-31-9P	169187-32-0P
	169187-33-1P	169187-34-2P	169187-35-3P	
	169187-36-4P	169187-37-5P	169187-38-6P	
	169187-39-7P	169187-40-0P	169187-41-1P	
	169187-42-2P	169187-43-3P	169187-44-4P	169187-45-5P
	169187-46-6P	169187-47-7P	169187-48-8P	
	169187-49-9P	169187-50-2P	169187-51-3P	
	169187-52-4P	169187-53-5P	169187-54-6P	169187-55-7P
	169187-56-8P	169187-57-9P	169187-58-0P	
	169187-59-1P	169187-60-4P	169187-61-5P	
	169187-62-6P	169187-63-7P	169187-64-8P	169187-65-9P
	169187-66-0P	169187-67-1P	169187-68-2P	
	169187-69-3P	169187-70-6P	169187-71-7P	169187-72-8P

169187-73-9P 169187-74-0P 169187-75-1P 169187-76-2P
 169187-77-3P 169187-78-4P 169187-79-5P 169187-80-8P
 169187-81-9P 169187-82-0P 169187-83-1P 169187-84-2P
 169187-85-3P 169187-86-4P 169187-87-5P 169187-88-6P
 169187-89-7P 169187-90-0P 169187-91-1P 169187-92-2P
 169187-93-3P 169187-94-4P 169187-95-5P 169187-96-6P
 169187-97-7P 169187-98-8P 169187-99-9P 169188-00-5P
 169188-01-6P 169188-02-7P 169188-03-8P 169188-04-9P
 169188-05-0P 169188-06-1P 169188-07-2P 169188-08-3P
 169188-09-4P 169188-10-7P 169188-11-8P 169188-12-9P
 169188-13-0P 169188-14-1P 169188-15-2P 169188-16-3P

ROLE: BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)

(preparation of N-(oxobenzazepinyl)alkanamides as growth
 hormone release promoters)

INDEX TERM: 169188-17-4P

ROLE: BYP (Byproduct); PREP (Preparation)
 (preparation of N-(oxobenzazepinyl)alkanamides as growth
 hormone release promoters)

INDEX TERM: 98-01-1, Furfuraldehyde, reactions 110-87-2 577-19-5,
 2-Bromo-1-nitrobenzene 620-02-0, 5-Methylfuran-2-
 carboxaldehyde 5720-05-8, 4-Tolylboronic acid
 10111-08-7, 2-Imidazolecarboxaldehyde 145485-77-4
 169188-19-6

ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of N-(oxobenzazepinyl)alkanamides as growth
 hormone release promoters)

INDEX TERM: 70680-21-6P 114772-39-3P 145457-11-0P 159814-82-1P
 159814-84-3P 159815-76-6P 159815-77-7P 159815-78-8P
 159815-79-9P 159815-80-2P 159815-81-3P 159815-82-4P
 159815-83-5P 169188-18-5P

ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation of N-(oxobenzazepinyl)alkanamides as growth
 hormone release promoters)

INDEX TERM: 12629-01-5, Human growth hormone

ROLE: BSU (Biological study, unclassified); MSC
 (Miscellaneous); BIOL (Biological study)
 (release; preparation of N-(oxobenzazepinyl)alkanamides as
 growth hormone release promoters)

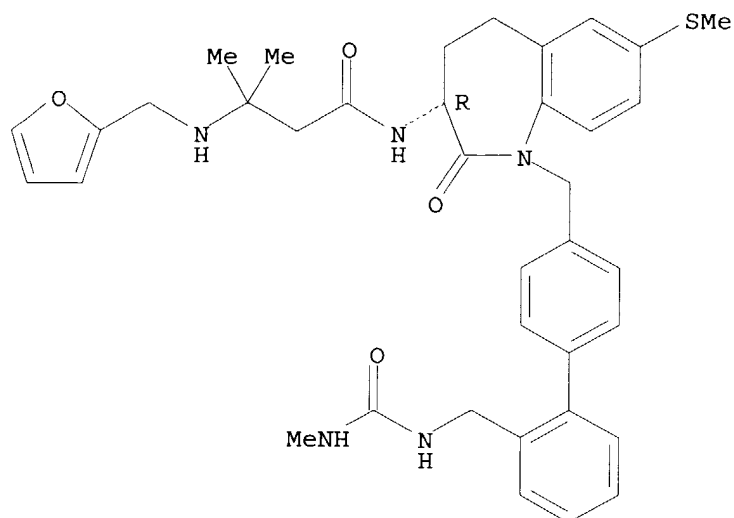
IT 169187-36-4P 169187-41-1P 169187-46-6P
 169187-51-3P 169187-56-8P 169187-61-5P
 169187-66-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of N-(oxobenzazepinyl)alkanamides as growth hormone release
 promoters)

RN 169187-36-4 HCAPLUS

CN Butanamide, 3-[(2-furanylmethyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-1-
 [[2'-[[[(methylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-
 (methylthio)-2-oxo-1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA INDEX NAME)

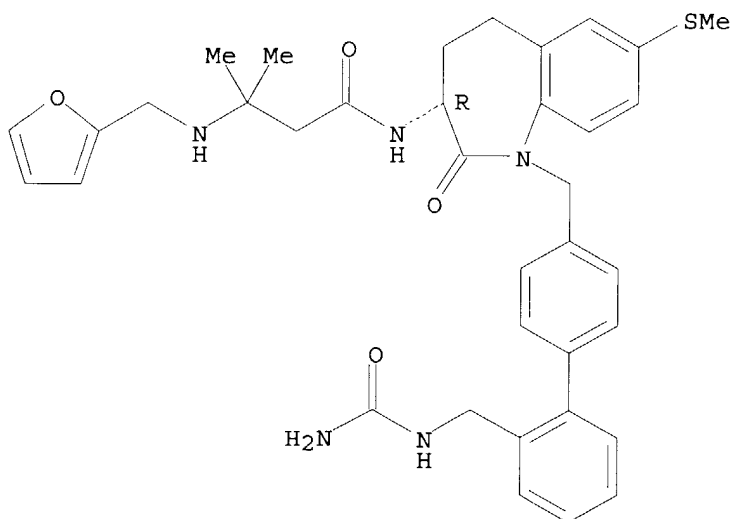
Absolute stereochemistry.



RN 169187-41-1 HCAPLUS

CN Butanamide, N-[1-[[2'-[[[(aminocarbonyl)amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-furanylmethyl)amino]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

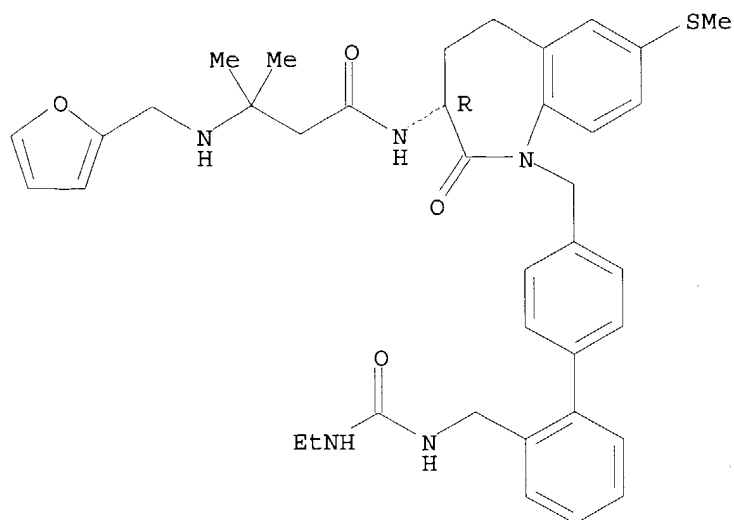
Absolute stereochemistry.



RN 169187-46-6 HCAPLUS

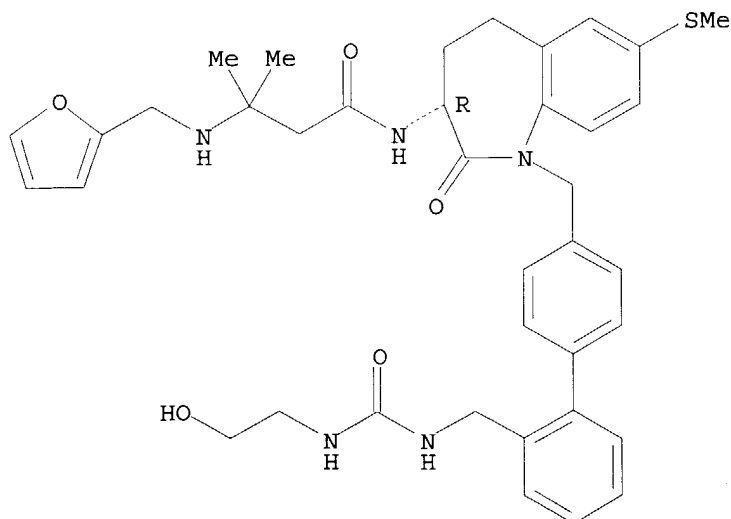
CN Butanamide, N-[1-[[2'-[[[(ethylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-furanylmethyl)amino]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



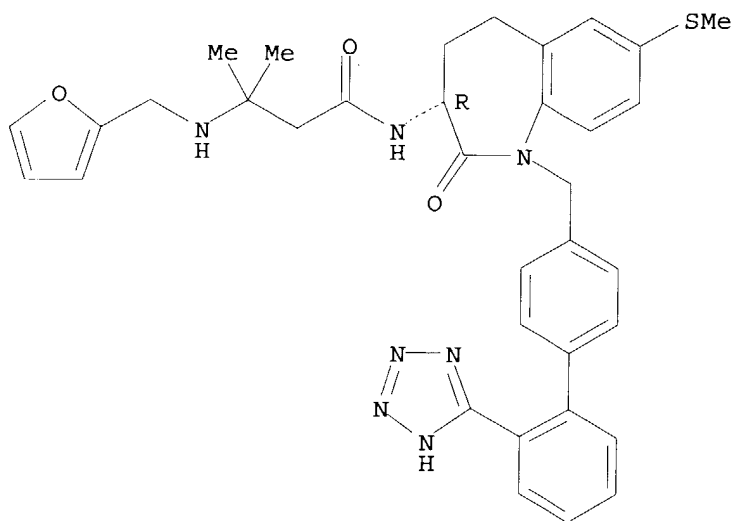
RN 169187-51-3 HCAPLUS
 CN Butanamide, 3-[(2-furanylmethyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-1-
 [[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-
 yl]methyl]-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



RN 169187-56-8 HCAPLUS
 CN Butanamide, 3-[(2-furanylmethyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-
 (methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-
 1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA INDEX NAME)

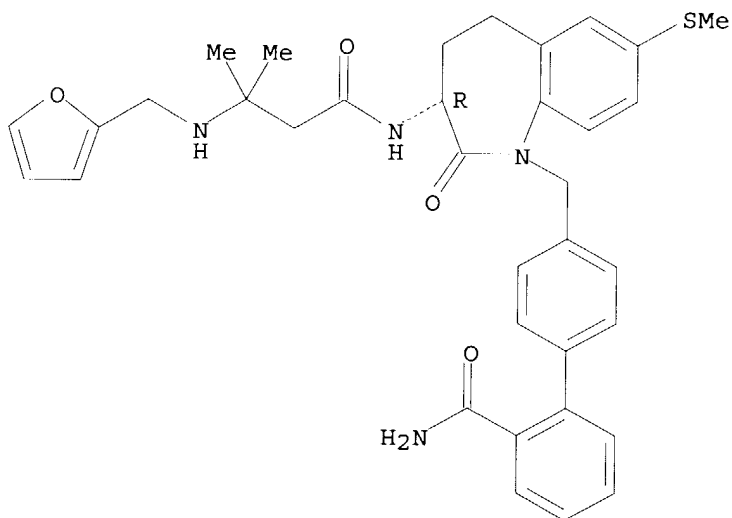
Absolute stereochemistry.



RN 169187-61-5 HCAPLUS

CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[3-[[3-[(2-furanylmethyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl]-, (R)- (9CI) (CA INDEX NAME)

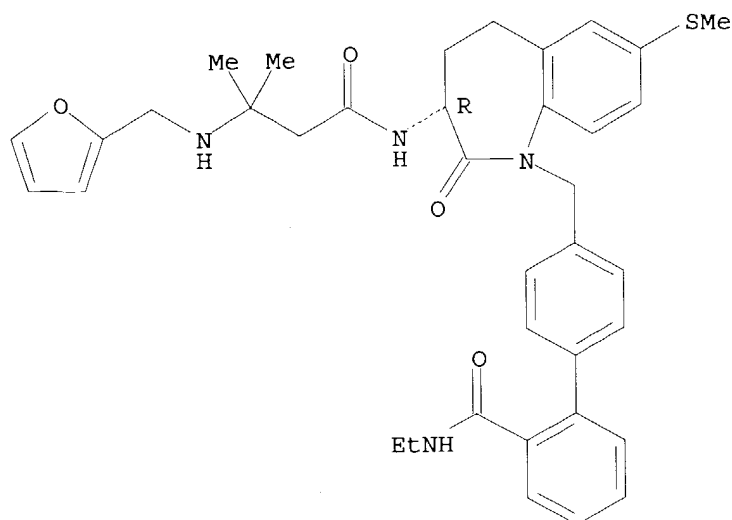
Absolute stereochemistry.



RN 169187-66-0 HCAPLUS

CN [1,1'-Biphenyl]-2-carboxamide, N-ethyl-4'-[[3-[[3-[(2-furanylmethyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



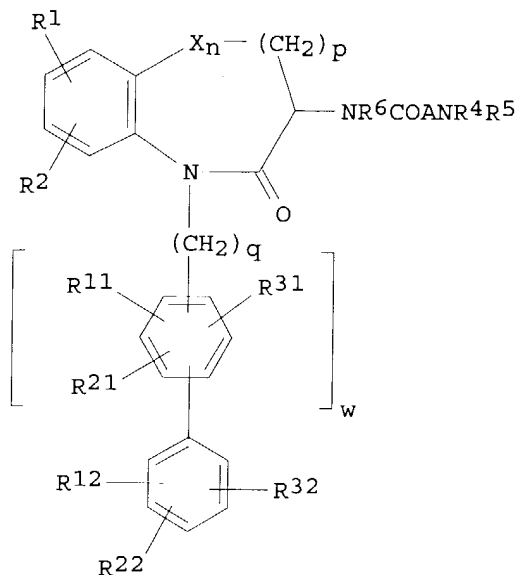
L52 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:867575 HCAPLUS
 DOCUMENT NUMBER: 123:256776
 ENTRY DATE: Entered STN: 20 Oct 1995
 TITLE: Preparation of benzo-fused lactams which promote release of growth hormone.
 INVENTOR(S): Schoen, William R.; Wyvratt, Matthew J., Jr.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: PCT Int. Appl., 131 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: C07D281-10
 SECONDARY: C07D223-16; C07D281-18; C07D223-06; A61K031-55
 CLASSIFICATION: 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 27
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9503289	A1	19950202	WO 1994-US8195	19940720
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5434261	A	19950718	US 1993-97149	19930726
AU 9474015	A1	19950220	AU 1994-74015	19940720
ZA 9405463	A	19950302	ZA 1994-5463	19940725
PRIORITY APPLN. INFO.:			US 1993-97149	A 19930726
			WO 1994-US8195	W 19940720

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
-----	-----	-----

WO 9503289 ICM C07D281-10
 ICS C07D223-16; C07D281-18; C07D223-06; A61K031-55
 US 5434261 ECLA C07D215/38C; C07D223/16B; C07D225/06; C07D267/14;
 C07D279/16; C07D281/10; C07D285/38; C07D040/12;
 C07D453/02; C07K005/06A1H
 OTHER SOURCE(S): MARPAT 123:256776
 GRAPHIC IMAGE:



ABSTRACT:

Title compds. [I; n, w = 0,1; p = 0-3; q = 0-4; X = CO, O, SOM, CH(OH), NR10, CH:CH; m = 0-2; R1, R2, R11, R12, R21, R22 = H, halo, alkyl, perfluoroalkyl, perfluoroalkoxy, cyano, NO2, (substituted) Ph, etc.; R31, R32 = H, R9, R9-substituted alkyl, Ph, PhO; R9 = R41R121NSO2(CH2)v, etc.; v = 1-3; R4, R5, R41 = H, (substituted) Ph, alkyl, alkenyl, alkynyl; R121 = R5, OR5, COR5, etc.; R4R5 = (CH2)rB(CH2)s; B = CHR1, O, SOM, NR10; r, s = 1-3; R6 = H, alkyl, Ph, phenylalkyl; A = (CH2)xCR8R81(CH2)y; x, y = 0-3; R8, R81 = H, alkyl, CF3, Ph (substituted) alkyl; R8R81 = (CH2)t; t = 2-6; R8, R81 can form alkylene bridges with R4 and/or R5], were prepared as promoters of the release of growth hormone in humans and animals (no data). Thus, 1-bromo-2-tert-butylbenzenesulfonamide (preparation given) and (4-methylphenyl)trimethylstannane (preparation given) were stirred with (Ph3P)2PdCl2 in DMF at 90° for 6 h to give 58% 4-methyl-2'-(tert-butylaminosulfonyl)-1,1'-biphenyl. This was refluxed with N-bromosuccinimide/azobisisobutyronitrile in CCl4 to give crude 4-bromomethyl-2'-(tert-butylaminosulfonyl)-1,1'-biphenyl. This was added to a mixture of 3-benzoyloxycarbonylamino-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepin-3(R)-yl]butanamide and NaH in DMF and the mixture was stirred 12 h to give 46% 3-benzoyloxycarbonylamino-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-1-[[2'-(tert-butylamino)sulfonyl[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3(R)-yl]butanamide. This was converted to title compound 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-1-[[2'-(benzamido)sulfonyl[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3(R)-yl]butanamide trifluoroacetate.

SUPPL. TERM: biphenylmethylbenzazepinone prepn growth hormone release

promoter; benzazepinone biphenylmethyl acylamino growth hormone promoter; obesity treatment benzazepinone biphenylmethyl acylamino; osteoporosis treatment benzazepinone biphenylmethyl acylamino; benzothiazepinone biphenylmethyl acylamino growth hormone promoter

INDEX TERM: Antiobesity agents
(benzo-fused lactam growth hormone release promoters with adrenergic agonists)

INDEX TERM: Peptides, biological studies
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(growth hormone releasing; GHRP-1, benzo-fused lactam growth hormone release promoters with other growth hormone secretagogues for increasing endogenous production of GH)

INDEX TERM: Peptides, biological studies
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(growth hormone releasing; GHRP-2, benzo-fused lactam growth hormone release promoters with other growth hormone secretagogues for increasing endogenous production of GH)

INDEX TERM: Osteoporosis
(treatment; benzo-fused lactam growth hormone release promoters with parathyroid hormone or a bisphosphonate)

INDEX TERM: Adrenergic antagonists
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α 2-, benzo-fused lactam growth hormone release promoters with adrenergic antagonists for treating obesity)

INDEX TERM: Adrenergic antagonists
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β 3-, benzo-fused lactam growth hormone release promoters with adrenergic antagonists for treating obesity)

INDEX TERM: 9034-39-3, Growth hormone releasing factor 36085-73-1, B-HT 920 67763-97-7, IGF-2 87616-84-0
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzo-fused lactam growth hormone release promoters with other growth hormone secretagogues for increasing endogenous production of GH)

INDEX TERM: 67763-96-6, IGF-1
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzo-fused lactam growth hormone release promoters with

other growth hormone secretagogues for increasing endogenous production of GH and treating the catabolic effects of nitrogen wasting)

INDEX TERM: 9002-64-6, Parathyroid hormone

ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(benzo-fused lactam growth hormone release promoters with parathyroid hormone or a bisphosphonate for treating osteoporosis)

INDEX TERM: 161517-58-4P 161517-59-5P 161517-60-8P 169188-20-9P
 169188-21-0P **169188-22-1P** 169188-23-2P
 169188-24-3P 169188-25-4P 169188-26-5P
169188-27-6P 169188-28-7P 169188-29-8P
 169188-30-1P 169188-31-2P **169188-32-3P**
 169188-33-4P 169188-34-5P 169188-35-6P 169188-36-7P
169188-37-8P 169188-38-9P 169188-39-0P
 169188-40-3P 169188-41-4P **169188-42-5P**
 169188-43-6P 169188-44-7P 169188-45-8P 169188-46-9P
169188-47-0P 169188-48-1P 169188-49-2P
 169188-50-5P 169188-51-6P **169188-52-7P**
 169188-53-8P 169188-54-9P 169188-55-0P 169188-56-1P
169188-57-2P 169188-58-3P 169188-59-4P
 169188-60-7P **169188-61-8P** 169188-62-9P
 169188-63-0P 169188-64-1P 169188-65-2P
169188-66-3P 169188-67-4P 169188-68-5P
 169188-69-6P 169188-70-9P **169188-71-0P**
 169188-72-1P 169188-73-2P 169188-74-3P 169188-75-4P
169188-76-5P 169188-77-6P 169188-78-7P
 169188-79-8P **169188-80-1P** 169188-81-2P
 169188-82-3P 169188-83-4P 169188-84-5P
169188-85-6P 169188-86-7P 169188-87-8P
 169188-88-9P 169188-89-0P **169188-90-3P**
 169188-91-4P 169188-92-5P 169188-93-6P 169188-94-7P
169188-95-8P 169188-96-9P 169188-97-0P
 169188-98-1P 169188-99-2P 169189-00-8P 169189-01-9P
 169189-02-0P 169189-03-1P 169189-04-2P 169189-05-3P
 169189-06-4P 169189-07-5P 169189-08-6P 169189-09-7P
 169189-10-0P 169189-11-1P 169189-12-2P 169189-13-3P
 169189-14-4P 169189-15-5P 169189-16-6P 169189-17-7P
 169189-18-8P 169189-19-9P 169189-20-2P 169189-21-3P
 169189-22-4P 169189-23-5P 169189-24-6P 169189-25-7P
 169189-26-8P 169189-27-9P 169189-28-0P 169189-29-1P
 169189-30-4P 169189-31-5P 169189-32-6P 169189-33-7P
 169189-34-8P 169189-35-9P 169189-36-0P 169189-37-1P
 169189-38-2P 169189-39-3P 169189-40-6P 169189-41-7P
 169189-42-8P 169189-43-9P 169189-44-0P 169189-45-1P
 169189-46-2P 169189-47-3P 169189-48-4P 169189-49-5P
 169189-50-8P 169189-51-9P 169189-52-0P 169189-53-1P
 169189-54-2P 169189-55-3P 169189-56-4P 169189-57-5P
 169189-58-6P 169189-59-7P 169189-60-0P 169189-61-1P
 169189-62-2P 169189-63-3P 169189-64-4P 169189-65-5P
 169189-66-6P 169189-67-7P 169189-68-8P 169189-69-9P
 169189-70-2P 169189-71-3P 169189-72-4P 169189-73-5P
 169189-74-6P 169189-75-7P 169189-76-8P 169189-84-8P
 169189-85-9P

ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of benzo-fused lactams which promote release of growth hormone)

INDEX TERM: 9002-72-6, Growth hormone
 ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (preparation of benzo-fused lactams which promote release of growth hormone)

INDEX TERM: 65-85-0, Benzoic acid, reactions 75-64-9, tert-Butylamine, reactions 557-66-4, Ethylamine hydrochloride 1066-45-1, Trimethyltin chloride 2905-25-1, o-Bromobenzenesulfonyl chloride 4294-57-9, p-Tolylmagnesium bromide 145457-70-1 145485-77-4
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of benzo-fused lactams which promote release of growth hormone)

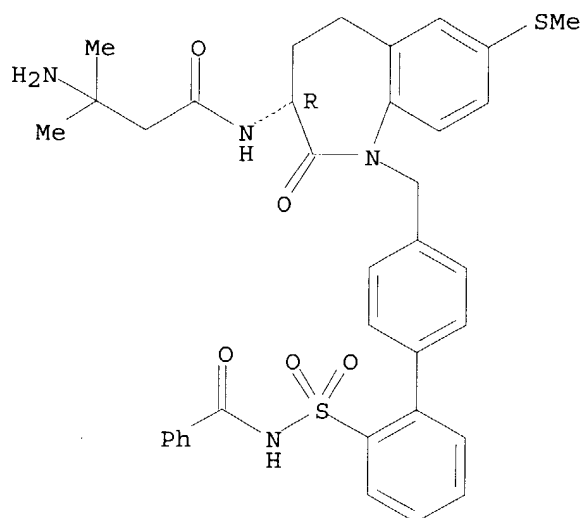
INDEX TERM: 937-12-2P 138733-50-3P 138733-51-4P 138733-52-5P 161517-55-1P 169189-78-0P 169189-79-1P 169189-80-4P 169189-81-5P 169189-82-6P 169189-83-7P
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of benzo-fused lactams which promote release of growth hormone)

IT 169188-22-1P 169188-27-6P 169188-32-3P 169188-37-8P 169188-42-5P 169188-47-0P 169188-52-7P 169188-57-2P 169188-61-8P 169188-66-3P 169188-71-0P 169188-76-5P 169188-80-1P 169188-85-6P 169188-90-3P 169188-95-8P
 RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of benzo-fused lactams which promote release of growth hormone)

RN 169188-22-1 HCAPLUS

CN Benzamide, N-[[4'-[[3-[(3-amino-3-methyl-1-oxobutyl)amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, (R)- (9CI) (CA INDEX NAME)

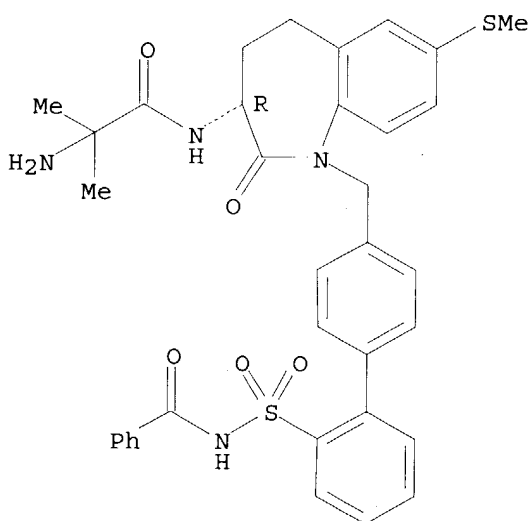
Absolute stereochemistry.



RN 169188-27-6 HCAPLUS

CN Benzamide, N-[[4'-[[3-[(2-amino-2-methyl-1-oxopropyl)amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, (R)- (9CI) (CA INDEX NAME)

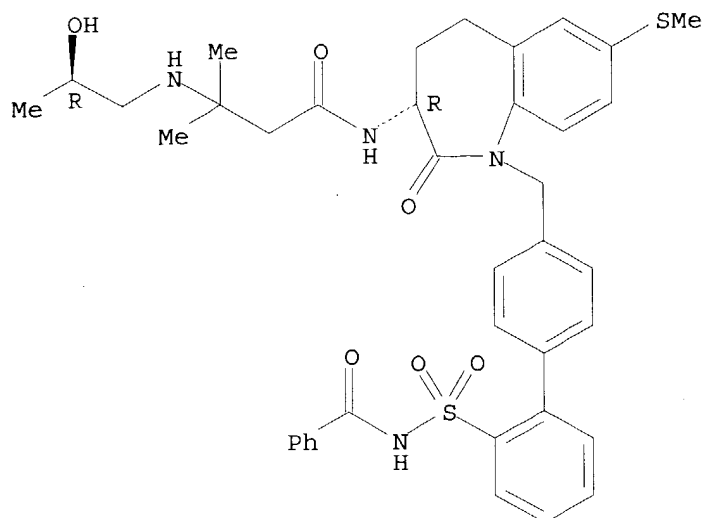
Absolute stereochemistry.



RN 169188-32-3 HCAPLUS

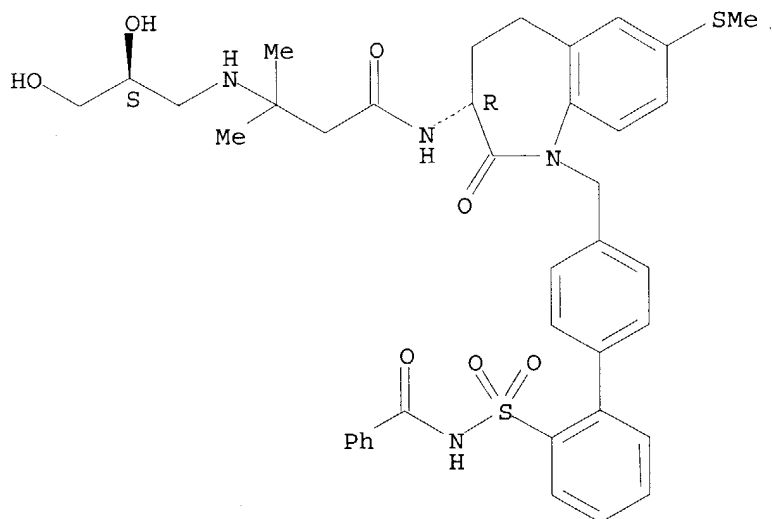
CN Benzamide, N-[[4'-[[2,3,4,5-tetrahydro-3-[[3-[(2-hydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



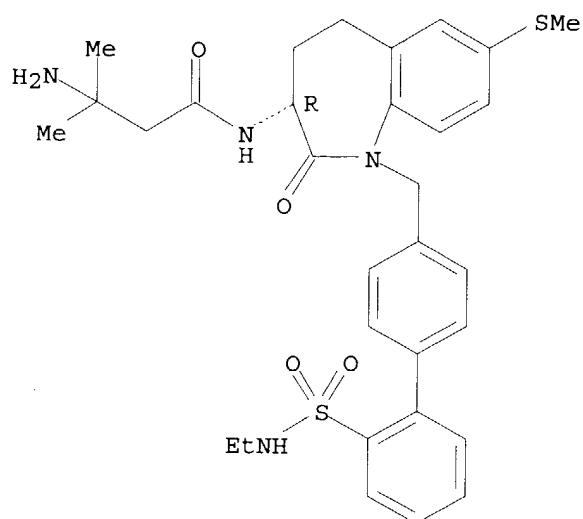
RN 169188-37-8 HCAPLUS
 CN Benzamide, N-[[4'-[[3-[[3-[(2,3-dihydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, [S-(R*,S*)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169188-42-5 HCAPLUS
 CN Butanamide, 3-amino-N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, (R)-(9CI) (CA INDEX NAME)

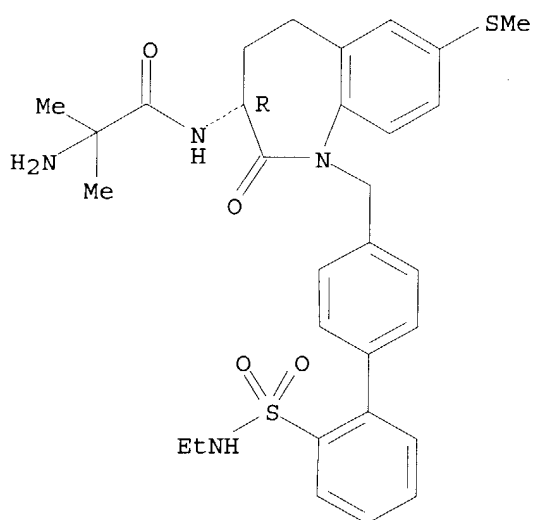
Absolute stereochemistry.



RN 169188-47-0 HCAPLUS

CN Propanamide, 2-amino-N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

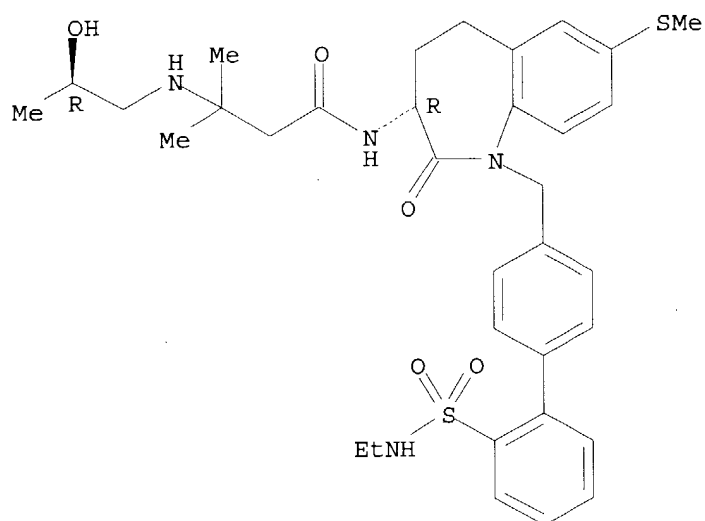
Absolute stereochemistry.



RN 169188-52-7 HCAPLUS

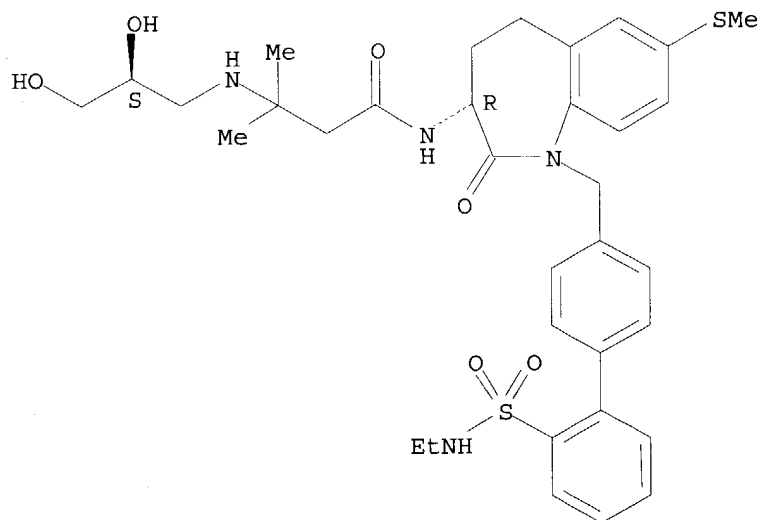
CN Butanamide, N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



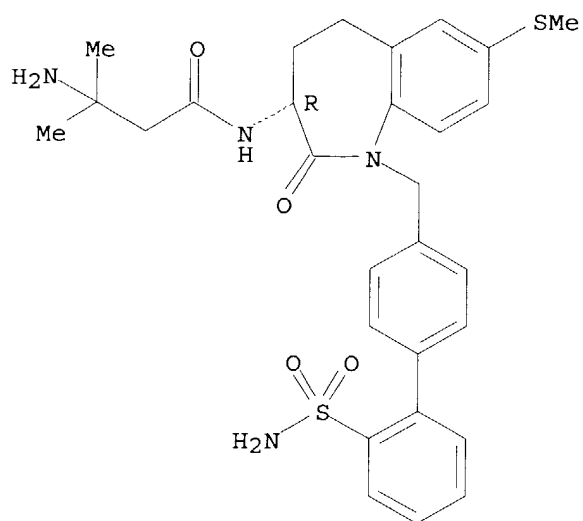
RN 169188-57-2 HCAPLUS
 CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, [S-(R*,S*)]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



RN 169188-61-8 HCAPLUS
 CN Butanamide, 3-amino-N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

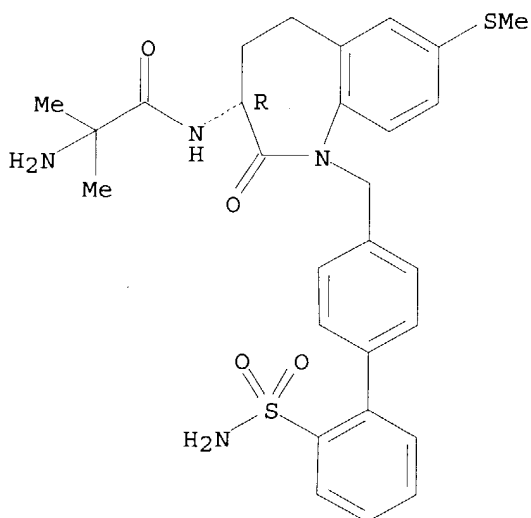
Absolute stereochemistry.



RN 169188-66-3 HCAPLUS

CN Propanamide, 2-amino-N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-2-methyl-, (R) - (9CI) (CA INDEX NAME)

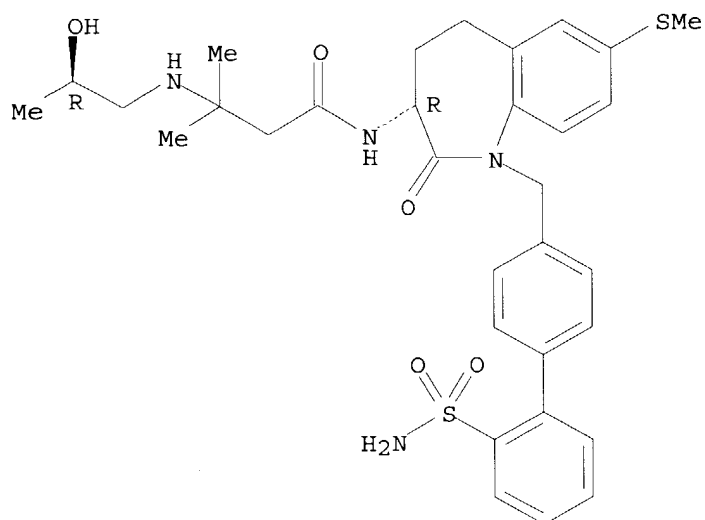
Absolute stereochemistry.



RN 169188-71-0 HCAPLUS

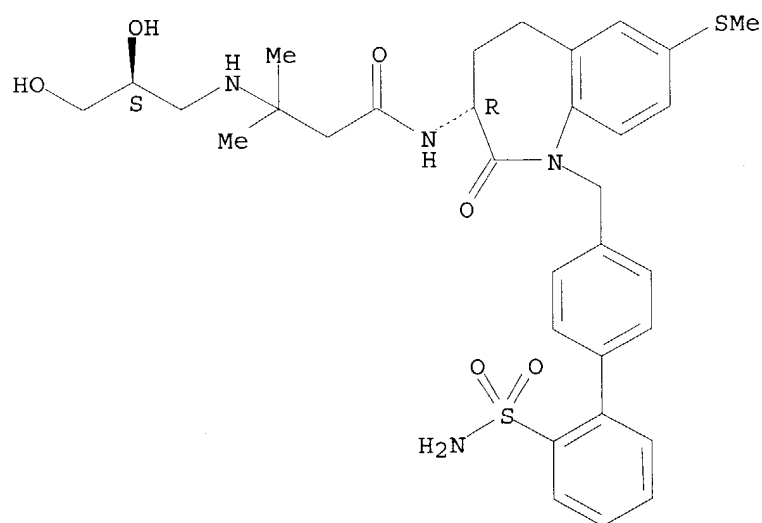
CN Butanamide, N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



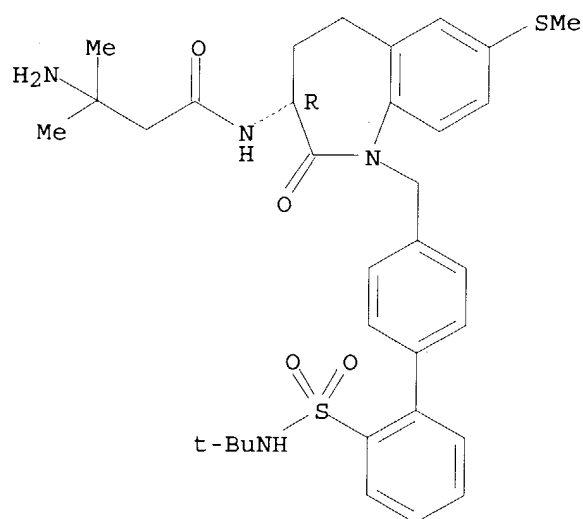
RN 169188-76-5 HCAPLUS
 CN Butanamide, N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2,3-dihydroxypropyl)amino]-3-methyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169188-80-1 HCAPLUS
 CN Butanamide, 3-amino-N-[1-[[2'-[[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

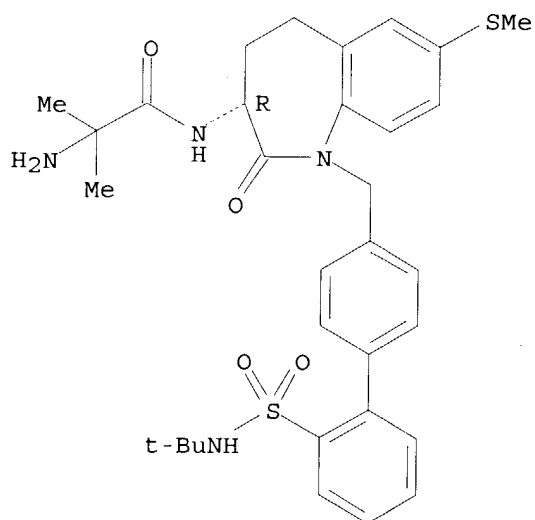
Absolute stereochemistry.



RN 169188-85-6 HCAPLUS

CN Propanamide, 2-amino-N-[1-[[2'-[[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

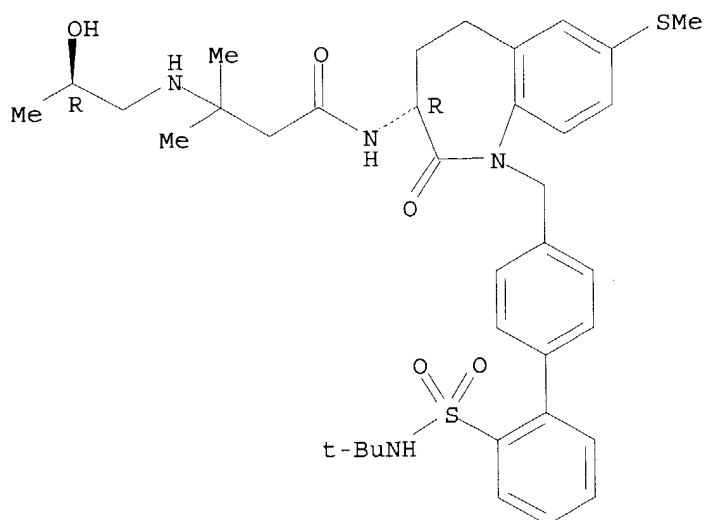
Absolute stereochemistry.



RN 169188-90-3 HCAPLUS

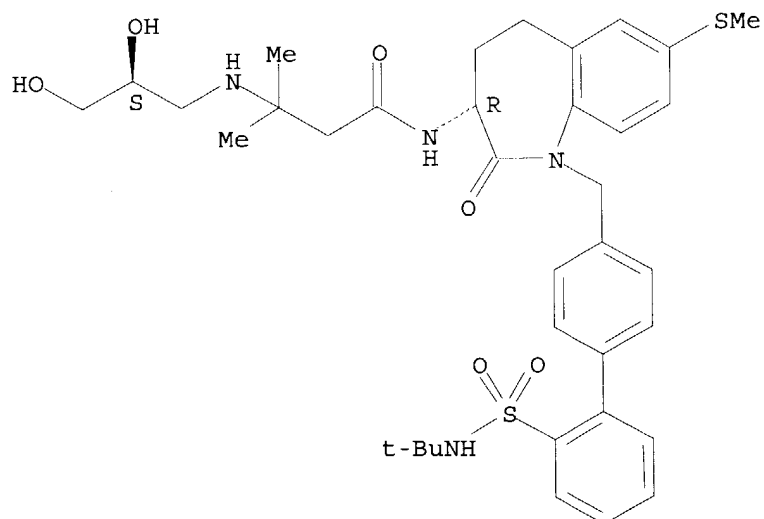
CN Butanamide, N-[1-[[2'-[[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169188-95-8 HCAPLUS
 CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-N-[1-[[2'-[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, [S-(R*,S*)] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



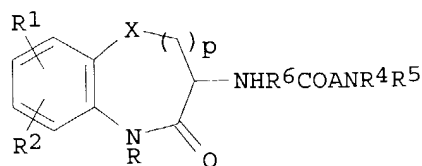
L52 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:792575 HCAPLUS
 DOCUMENT NUMBER: 123:198644
 ENTRY DATE: Entered STN: 15 Sep 1995
 TITLE: Preparation of N-(N-heterocyclylbenzazepinyl)aminoalka
 namides as growth hormone release promoters
 INVENTOR(S): Schoen, William R.; Wyvratt, Matthew J.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 174 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: A61K031-555
 SECONDARY: A61K031-395; C07D403-06; C07D401-06; C07D405-06;
 C07D413-06
 CLASSIFICATION: 27-21 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

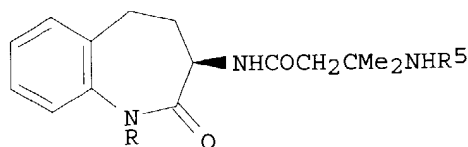
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9408583	A1	19940428	WO 1993-US9561	19931005
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5374721	A	19941220	US 1992-961008	19921014
CA 2144764	AA	19940428	CA 1993-2144764	19931005
AU 9453226	A1	19940509	AU 1994-53226	19931005
AU 676223	B2	19970306		
EP 665750	A1	19950809	EP 1993-923288	19931005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08502297	T2	19960312	JP 1993-510111	19931005
ZA 9307594	A	19940503	ZA 1993-7594	19931013
US 5726307	A	19980310	US 1994-356935	19941215
PRIORITY APPLN. INFO.:			US 1992-961008	A1 19921014
			WO 1993-US9561	W 19931005

PATENT CLASSIFICATION CODES:

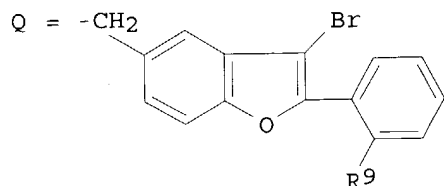
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9408583	ICM	A61K031-555
	ICS	A61K031-395; C07D403-06; C07D401-06; C07D405-06; C07D413-06
US 5374721	ECLA	C07D403/06; C07D403/14; C07D405/06; C07D405/14; C07D049/06; C07D409/14; C07D413/06
OTHER SOURCE(S):		MARPAT 123:198644
GRAPHIC IMAGE:		



I



II



ABSTRACT:

Title compds. [I; A = (un)substituted alkylene; R = (CH₂)_qLR₇; L = (un)substituted divalent benzo-fused heterocyclyl; R₁,R₂ = H, halo, (perfluoro)alkyl, Ph, etc.; R₄,R₅ = H, alkyl, Ph, etc.; R₆ = H, alkyl, phenyl(alkyl); R₇ = (un)substituted Ph; X = CO, O, SOO-2, CH(OH), CH:CH, etc.; n = 0 or 1; p = 0-3; q = 0-4] were prepared as growth hormone release promoters (no data). Thus, 1-tetralone was converted in 5 steps to 3(R)-amino-2,3,4,5-tetrahydro-1H-benzazepin-2-one which was amidated by HO₂CCH₂CMe₂NHBOC (preparation given) to give benzazepinylaminoalkanamide II (R = H, R₅ = BOC) which was N-alkylated by BrCH₂LR₇ (CH₂LR₇ = benzofuranylmethyl group Q, R₉ = trityl-protected 5-tetrazolyl) to give, after deprotection, II (R = Q, R₅ = H, R₉ = 5-tetrazolyl).

SUPPL. TERM: benzazepinylaminoalkanamide growth hormone release
 INDEX TERM: Antiobesity agents
 (preparation of N-(N-heterocyclylbenzazepinyl)aminoalkanamides
 as growth hormone release promoters)
 INDEX TERM: Osteoporosis
 (treatment; preparation of N-(N-heterocyclylbenzazepinyl)amino
 alkanamides as growth hormone release promoters)
 INDEX TERM: 613-84-3P 3349-64-2P, 1-Tetralone oxime 4424-80-0P
 4879-95-2P 86499-35-6P 129765-95-3P 137036-55-6P
 140700-64-7P 143381-79-7P 143381-80-0P 143381-81-1P
 145457-69-8P 145485-77-4P 145486-33-5P 145486-47-1P
 155300-46-2P 160278-26-2P 164802-91-9P 167710-92-1P
 167710-93-2P 167823-28-1P
 ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of N-(N-
 heterocyclylbenzazepinyl)aminoalkanamides as growth
 hormone release promoters)
 INDEX TERM: 167822-21-1P 167822-22-2P 167822-23-3P 167822-24-4P
 167822-25-5P 167822-26-6P 167822-27-7P 167822-28-8P
 167822-29-9P 167822-30-2P 167822-31-3P 167822-32-4P
 167822-33-5P 167822-34-6P 167822-35-7P 167822-36-8P
 167822-37-9P 167822-38-0P 167822-39-1P 167822-40-4P

167822-41-5P 167822-42-6P 167822-43-7P 167822-44-8P
 167822-45-9P 167822-46-0P 167822-47-1P 167822-48-2P
 167822-49-3P 167822-50-6P 167822-51-7P 167822-52-8P
 167822-53-9P 167822-54-0P 167822-55-1P 167822-56-2P
 167822-57-3P 167822-58-4P 167822-59-5P 167822-60-8P
 167822-61-9P 167822-62-0P 167822-63-1P 167822-64-2P
 167822-65-3P 167822-66-4P 167822-67-5P 167822-68-6P
 167822-69-7P 167822-70-0P 167822-71-1P 167822-72-2P
 167822-73-3P **167822-74-4P** 167822-75-5P
 167822-76-6P 167822-77-7P 167822-78-8P 167822-79-9P
 167822-80-2P 167822-81-3P 167822-82-4P 167822-83-5P
 167822-84-6P 167822-85-7P 167822-86-8P 167822-87-9P
 167822-88-0P 167822-89-1P 167822-90-4P 167822-91-5P
 167822-92-6P 167822-93-7P 167822-94-8P 167822-95-9P
 167822-96-0P **167822-97-1P** 167822-98-2P
 167822-99-3P 167823-00-9P 167823-01-0P 167823-02-1P
 167823-03-2P 167823-04-3P 167823-05-4P 167823-06-5P
 167823-07-6P 167823-08-7P 167823-09-8P 167823-10-1P
 167823-11-2P 167823-12-3P 167823-13-4P 167823-14-5P
 167823-15-6P 167823-16-7P 167823-17-8P 167823-18-9P
 167823-19-0P 167823-20-3P 167823-21-4P 167823-22-5P
 167823-23-6P 167823-24-7P 167823-25-8P 167823-26-9P

ROLE: BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)

INDEX TERM:

(preparation of N-(N-heterocyclylbenzazepinyl)aminoalkanamides
 as growth hormone release promoters)
 9002-72-6, Growth hormone

ROLE: BPR (Biological process); BSU (Biological study,
 unclassified); MSC (Miscellaneous); BIOL (Biological study);
 PROC (Process)

INDEX TERM:

(preparation of N-(N-heterocyclylbenzazepinyl)aminoalkanamides
 as growth hormone release promoters)

106-44-5, reactions 115-11-7, reactions 529-34-0,
 1-Tetralone 22115-41-9, α -Bromo-o-tolunitrile
 81445-45-6

ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (starting material; preparation of N-(N-
 heterocyclylbenzazepinyl)aminoalkanamides as growth
 hormone release promoters)

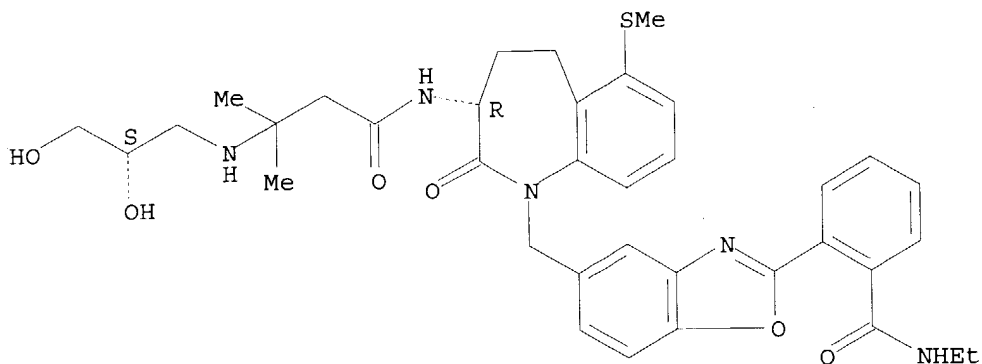
IT **167822-74-4P 167822-97-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of N-(N-heterocyclylbenzazepinyl)aminoalkanamides as growth
 hormone release promoters)

RN 167822-74-4 HCAPLUS

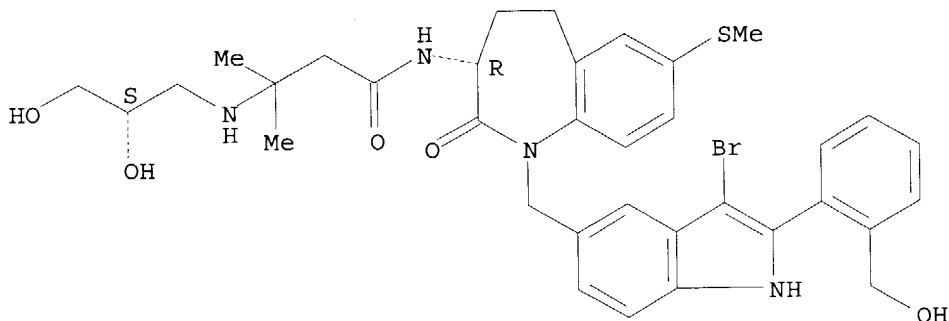
CN Benzamide, 2-[5-[[3-[[3-[(2,3-dihydroxypropyl)amino]-3-methyl-1-
 oxobutyl]amino]-2,3,4,5-tetrahydro-6-(methylthio)-2-oxo-1H-1-benzazepin-1-
 yl)methyl]-2-benzoxazolyl]-N-ethyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 167822-97-1 HCAPLUS
 CN Butanamide, N-[1-[[3-bromo-2-[2-(hydroxymethyl)phenyl]-1H-indol-5-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2,3-dihydroxypropyl)amino]-3-methyl-, [S-(R*,S*)] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



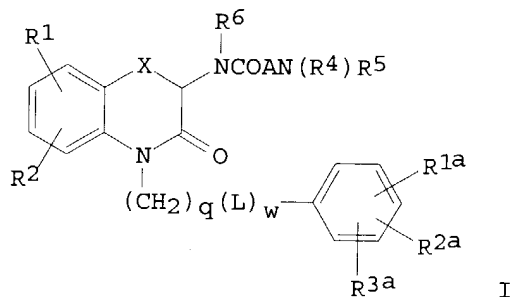
L52 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1995:9058 HCAPLUS
 DOCUMENT NUMBER: 122:160643
 ENTRY DATE: Entered STN: 08 Nov 1994
 TITLE: Benzo-fused lactams which promote the release of growth hormone
 INVENTOR(S): Ok, Ok Hyun; Schoen, William R.; Wyvratt, Matthew J.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: PCT Int. Appl., 133 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: A61K031-33
 SECONDARY: A61K031-55; C07D223-16; C07D225-06; C07D261-20; C07D267-02; C07D267-22; C07D281-02; C07D281-18
 CLASSIFICATION: 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407483	A1	19940414	WO 1993-US8894	19930921
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5317017	A	19940531	US 1992-954220	19920930
EP 665747	A1	19950809	EP 1993-922263	19930921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08502252	T2	19960312	JP 1993-509125	19930921
AU 676501	B2	19970313	AU 1993-51327	19930921
AU 9351327	A1	19940426		
ZA 9307222	A	19940420	ZA 1993-7222	19930929
PRIORITY APPLN. INFO.:			US 1992-954220	A1 19920930
			WO 1993-US8894	W 19930921

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9407483	ICM	A61K031-33
	ICS	A61K031-55; C07D223-16; C07D225-06; C07D261-20; C07D267-02; C07D267-22; C07D281-02; C07D281-18
		MARPAT 122:160643

OTHER SOURCE(S):
GRAPHIC IMAGE:



ABSTRACT:

The title compds. [I; A = (un)substituted alkylene; L = (un)substituted phenylene; R1, R1a, R2, R2a = H, halogen, C1-7 alkyl CN, NO2, (un)substituted Ph, etc.; R3a = H, (un)substituted C1-6 alkyl or Ph; R4, R5 = H, (un)substituted Ph, (un)substituted alkyl, alkenyl, alkynyl, etc.; R6 = H, C1-10 alkyl, Ph, phenyl-substituted alkyl; X = (un)substituted CH2CH2, (un)substituted CH:CH, etc.; q = 0-4; w = 0, 1], which promote the release the growth hormone (no data), are prepared Thus, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-4-(4-methoxyphenyl)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]butanamide trifluoroacetate was prepared from 2,3,4,5-tetrahydro-3-(methoxycarbonyl)-4-(4-methoxyphenyl)-1H-1-benzazepin-2-one in 14 steps.

SUPPL. TERM:

INDEX TERM:

tetrazolylbenzazepine growth hormone release stimulator
Lactams
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)
(benzo-fused, preparation of, as growth hormone release

accelerators)
INDEX TERM: 9002-72-6, Growth hormone
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(accelerated secretion of, benzo-fused lactams for)
INDEX TERM: 158103-83-4 158103-91-4 158103-93-6 158103-96-9
158103-99-2 158104-07-5 158104-08-6 158104-09-7
158104-10-0 158104-11-1
158104-12-2 158104-13-3 158104-14-4
158104-15-5 158104-16-6 158104-17-7 158104-18-8
158104-19-9 158104-20-2 **158104-21-3**
158104-22-4 158104-23-5 158104-24-6 158104-25-7
158104-26-8 158104-27-9 158104-28-0 158104-29-1
158104-30-4 **158104-31-5** 158104-32-6
158104-33-7 158104-34-8 158104-35-9 158104-36-0
158104-37-1 158104-38-2 158104-39-3 158104-40-6
158104-41-7 **158104-42-8** 158104-43-9
158104-44-0 158104-45-1 158104-46-2 158104-47-3
158104-48-4 158104-49-5 158104-50-8 158104-51-9
158104-52-0 158104-53-1 158104-54-2 158104-55-3
158104-56-4 158104-57-5 158104-58-6 158104-59-7
158104-60-0 158104-61-1 158104-62-2 158104-63-3
158104-64-4 158104-65-5 158104-66-6 158104-67-7
158104-68-8 158104-69-9 158104-70-2 158104-71-3
158104-72-4 158104-73-5 158104-74-6 158104-75-7
158104-76-8 158104-77-9 158104-78-0 158104-79-1
158104-80-4 158104-81-5 158104-82-6 158104-83-7
158104-84-8 158104-85-9 158104-86-0 158104-87-1
158104-88-2 158104-89-3 158104-90-6 158104-91-7
158104-92-8 158104-93-9 158104-94-0 158104-95-1
158124-30-2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(growth hormone release accelerator)
INDEX TERM: 9034-39-3, Growth hormone releasing factor 36085-73-1,
B-HT 920 67763-96-6, Insulin-like growth factor I
67763-97-7, Insulin-like growth factor II 87616-84-0, GHRP
6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(growth hormone secretagogue, benzo-fused lactams for
formulation with)
INDEX TERM: 4879-95-2P 18039-42-4P 87268-78-8P 104479-28-9P
129765-95-3P 133051-88-4P 133909-97-4P 155300-46-2P
158103-85-6P 158103-86-7P 158103-87-8P 158103-88-9P
158103-89-0P 158103-90-3P 158103-98-1P 158104-01-9P
158104-02-0P 158104-06-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of growth hormone
release accelerators)
INDEX TERM: 158103-84-5P 158103-92-5P 158103-94-7P 158103-97-0P
158104-00-8P 158104-04-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as growth hormone release accelerator)
INDEX TERM: 76-83-5, Triphenylmethyl chloride 100-47-0, Benzonitrile,
reactions 115-11-7, Isobutylene, reactions 624-31-7,
4-Iodotoluene 16029-98-4, Trimethylsilyl iodide
19832-98-5, 4-Methyl-1-tetralone 24424-99-5, Di-tert-butyl
dicarbonate 27068-88-8 81445-45-6 107967-07-7
158103-95-8
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of growth hormone release

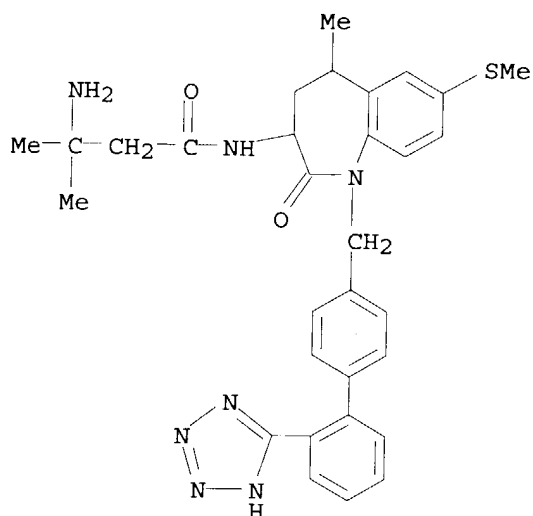
accelerators)

IT 158104-10-0 158104-11-1 158104-12-2

158104-21-3 158104-31-5 158104-42-8

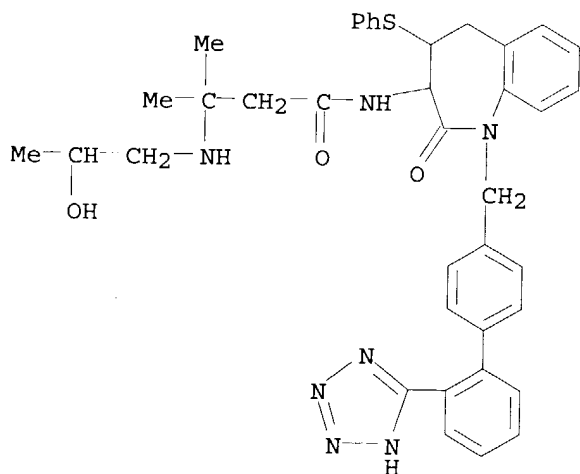
RL: RCT (Reactant); RACT (Reactant or reagent)
(growth hormone release accelerator)

RN 158104-10-0 HCAPLUS

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-5-methyl-7-(methylthio)-
2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-
benzazepin-3-yl]- (9CI) (CA INDEX NAME)

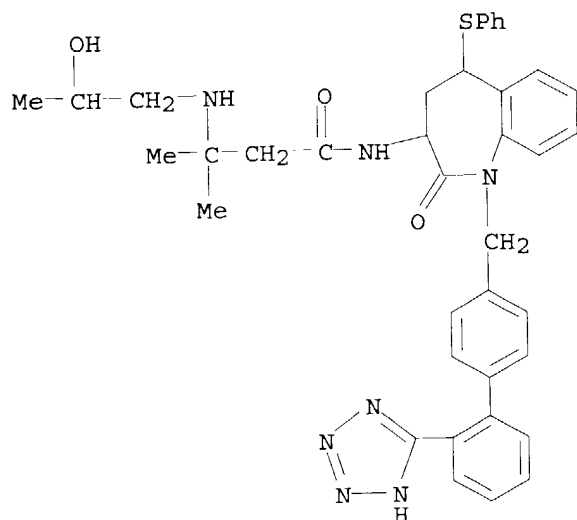
RN 158104-11-1 HCAPLUS

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-4-(phenylthio)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]- (9CI) (CA INDEX NAME)

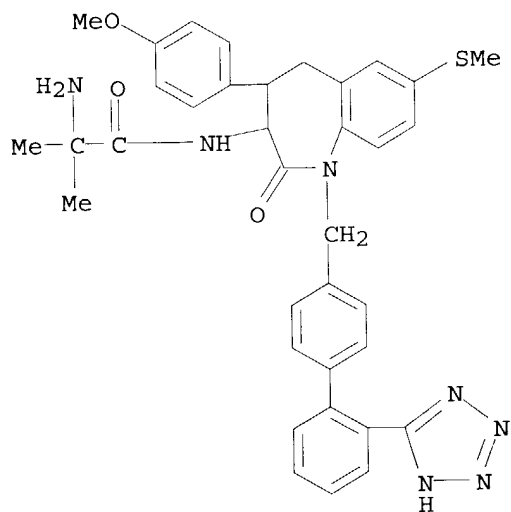


RN 158104-12-2 HCAPLUS

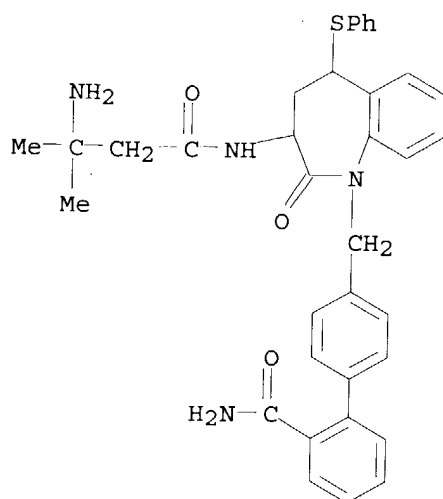
CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-5-(phenylthio)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]- (9CI) (CA INDEX NAME)



RN 158104-21-3 HCAPLUS
 CN Propanamide, 2-amino-2-methyl-N-[2,3,4,5-tetrahydro-4-(4-methoxyphenyl)-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]- (9CI) (CA INDEX NAME)

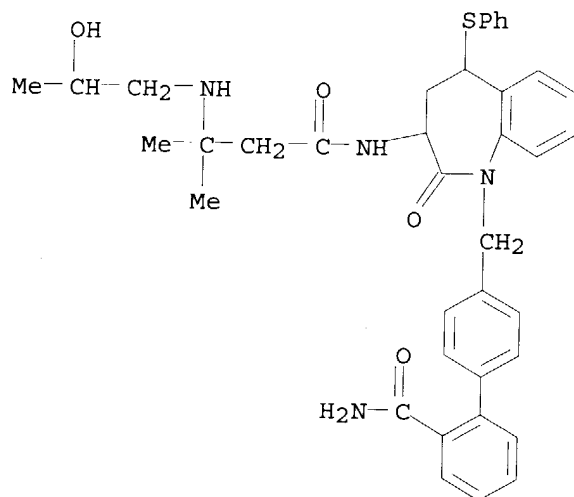


RN 158104-31-5 HCAPLUS
 CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[3-[(3-amino-3-methyl-1-oxobutyl)amino]-2,3,4,5-tetrahydro-2-oxo-5-(phenylthio)-1H-1-benzazepin-1-yl]methyl]- (9CI) (CA INDEX NAME)



RN 158104-42-8 HCAPLUS

CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[2,3,4,5-tetrahydro-3-[[3-[(2-hydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-2-oxo-5-(phenylthio)-1H-1-benzazepin-1-yl]methyl]- (9CI) (CA INDEX NAME)



L52 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:169109 HCAPLUS

DOCUMENT NUMBER: 118:169109

ENTRY DATE: Entered STN: 01 May 1993

TITLE: Preparation of (tetrazolylbiphenylmethyl)benzazepinone
s and related compounds as growth hormone release
promoters

INVENTOR(S): Fisher, Michael H.; Wyvratt, Matthew J.; Schoen,
William R.; Devita, Robert J.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 346 pp.

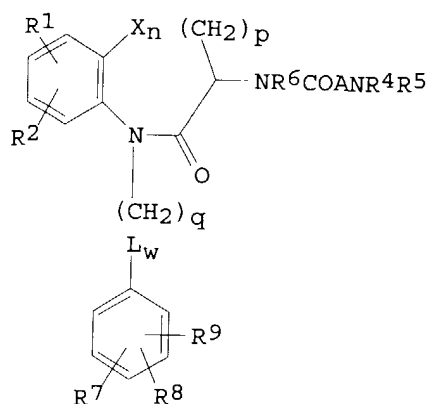
CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: C07D403-10
 SECONDARY: C07D223-16; C07D401-10; C07D417-10; C07D227-10;
 C07K005-06; C07D281-10; A61K031-33
 CLASSIFICATION: 28-10 (Heterocyclic Compounds (More Than One Hetero
 Atom))
 Section cross-reference(s): 1, 34
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9216524	A1	19921001	WO 1992-US2271	19920319
W: BB, BG, BR, LK, MG, MN, MW, PL, RO, RU, SD				
US 5206235	A	19930427	US 1992-839742	19920228
EP 513974	A1	19921119	EP 1992-302143	19920312
EP 513974	B1	19960904		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
AT 142206	E	19960915	AT 1992-302143	19920312
IL 101206	A1	19970218	IL 1992-101206	19920312
CA 2063185	AA	19920921	CA 1992-2063185	19920317
NO 9201077	A	19920921	NO 1992-1077	19920319
AU 9213012	A1	19920924	AU 1992-13012	19920319
AU 653992	B2	19941020		
CN 1066070	A	19921111	CN 1992-102954	19920319
CN 1033584	B	19961218		
ZA 9202009	A	19921125	ZA 1992-2009	19920319
JP 06172316	A2	19940621	JP 1992-112069	19920319
JP 08000814	B4	19960110		
HU 66796	A2	19941228	HU 1992-915	19920319
RO 117326	B1	20020130	RO 1993-1245	19920319
US 5310737	A	19940510	US 1993-12190	19930202
PRIORITY APPLN. INFO.:			US 1991-673695	A 19910320
			US 1992-839742	A 19920228
			WO 1992-US2271	W 19920319

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9216524	ICM	C07D403-10
	ICS	C07D223-16; C07D401-10; C07D417-10; C07D227-10; C07K005-06; C07D281-10; A61K031-33
OTHER SOURCE(S):		MARPAT 118:169109
GRAPHIC IMAGE:		



I

ABSTRACT:

Title compds. [I; L = (substituted) phenylene; n, w = 0, 1; p = 0-3; q = 0-4; X = CO, O, S, SO, SO₂, CH(OH), CH:CH, imino; R₁, R₂, R₇, R₈ = H, halo, (perfluoro)alkyl, perfluoroalkoxy, cyano, NO₂, (substituted) Ph, acyl(alkyl), etc.; R₄, R₅ = H, (substituted) Ph, alkyl, alkenyl, alkynyl, alkanoyloxy, alkoxycarbonyl, carboxy, CHO, amino; R₄R₅ = (CH₂)_rB(CH₂)_s; B = CH₂, O, imino, S, SO, SO₂; r, s = 1-3; R₆ = H, alkyl, Ph, phenylalkyl; R₉ = H, (substituted) tetrazolyl, acylalkyl, aminoalkyl, carbamoylalkyl, tetrazolylalkyl, tetrazolylphenyl, tetrazolylphenoxy, etc.; A = (CH₂)_xCR₁₀R₁₁(CH₂)_y; x, y = 0-3; R₁₀, R₁₁ = H, CF₃, (substituted) alkyl, Ph, etc.; R₁₀R₁₁ = (CH₂)_t; t = 2-6; R₁₀, R₁₁ may be joined to R₄ and/or R₅], were prepared for promotion of release of growth hormone (no data). Thus, 3-benzyloxycarbonylamino-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepin-3R-yl]butanamide (preparation from 3-azido-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one given) was stirred 15 min with NaH in DMF; N-triphenylmethyl-5-[2-(4'-bromobiphen-4-yl)]tetrazole (preparation starting from 5-phenyl-2-trityltetrazole and 4-IC₆H₄Me given) in DMF was added and the mixture was stirred 90 min to give 95% coupling product, which was hydrogenated in MeOH over Pd(OH)₂/C for 14 h to give 89% 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3R-yl]butanamide trifluoroacetate.

SUPPL. TERM: biphenylmethyloxobenzazepinamide growth hormone release;
benzazepinamide prepn growth hormone release

INDEX TERM:

145455-23-8P	145455-24-9P	145455-25-0P	145455-26-1P
145455-27-2P	145455-28-3P	145455-29-4P	145455-30-7P
145455-31-8P	145455-32-9P	145455-33-0P	145455-34-1P
145455-35-2P	145455-36-3P	145455-37-4P	145455-38-5P
145455-39-6P	145455-40-9P	145455-41-0P	145455-42-1P
145455-43-2P	145455-44-3P	145455-45-4P	145455-46-5P
145455-47-6P	145455-48-7P	145455-49-8P	145455-50-1P
145455-51-2P	145455-52-3P	145455-53-4P	145455-54-5P
145455-55-6P	145455-56-7P	145455-57-8P	145455-58-9P
145455-59-0P	145455-60-3P	145455-61-4P	145455-62-5P
145455-63-6P	145455-64-7P	145455-65-8P	145455-66-9P
145455-67-0P	145455-68-1P	145455-69-2P	
145455-70-5P	145455-71-6P		
145455-72-7P	145455-73-8P	145455-74-9P	
145455-75-0P	145455-76-1P	145455-77-2P	145455-78-3P
145455-79-4P	145455-80-7P	145455-81-8P	145455-83-0P
145455-84-1P	145455-85-2P	145455-87-4P	145455-88-5P
145455-90-9P	145455-92-1P	145455-94-3P	145455-96-5P
145455-98-7P	145456-00-4P	145456-02-6P	145456-04-8P

145456-06-0P	145456-08-2P	145456-09-3P	145456-11-7P
145456-12-8P	145456-14-0P	145456-16-2P	145456-17-3P
145456-18-4P	145456-19-5P	145456-20-8P	145456-22-0P
145456-24-2P	145456-26-4P	145456-28-6P	145456-30-0P
145456-31-1P	145456-33-3P	145456-35-5P	145456-37-7P
145456-39-9P	145456-41-3P	145456-42-4P	145456-44-6P
145456-46-8P	145456-48-0P	145456-50-4P	145456-52-6P
145456-54-8P	145456-56-0P	145456-57-1P	145456-59-3P
145456-60-6P	145456-62-8P	145456-64-0P	145456-65-1P
145456-67-3P	145456-69-5P	145456-70-8P	145456-71-9P
145456-72-0P	145456-73-1P	145456-74-2P	145456-75-3P
145456-76-4P	145456-78-6P	145456-80-0P	145456-82-2P
145456-84-4P	145456-86-6P	145456-87-7P	145456-88-8P
145456-90-2P	145456-92-4P	145456-93-5P	145456-95-7P
145456-97-9P	145456-99-1P	145457-01-8P	145457-03-0P
145457-05-2P	145457-07-4P	145457-08-5P	145457-09-6P
145457-11-0P	145457-13-2P	145457-15-4P	145457-17-6P
145457-19-8P	145457-21-2P	145457-23-4P	145457-24-5P
145457-26-7P	145457-28-9P	145457-30-3P	145457-31-4P
145457-33-6P	145457-35-8P	145457-37-0P	145457-39-2P
145457-41-6P	145457-42-7P	145457-44-9P	145457-46-1P
145457-48-3P	145457-50-7P	145457-52-9P	145457-54-1P
145457-55-2P	145457-57-4P	145457-58-5P	145457-60-9P
145457-62-1P	145457-64-3P	145457-66-5P	145457-68-7P
145484-87-3P	145484-88-4P	145484-89-5P	145484-90-8P
145484-91-9P	145484-92-0P	145484-93-1P	145484-95-3P
145484-97-5P	145484-99-7P	145486-76-6P	145486-78-8P
145552-83-6P	145552-84-7P	145552-86-9P	145552-88-1P
145552-90-5P	145552-92-7P	145552-94-9P	145552-96-1P

145552-97-2P 145552-98-3P 145554-00-3P

145632-40-2P 148350-69-0P 148350-70-3P 148378-64-7P
 ROLE: BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)

(preparation of, as growth hormone release promoter)

INDEX TERM:

145486-79-9

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(preparation of, as intermediate for growth hormone release
 promoter)

INDEX TERM:

937-12-2P	2052-07-5P	2840-44-0P	3349-64-2P
4424-80-0P	16927-79-0P	17174-96-8P	18039-42-4P
21259-96-1P	22009-40-1P	22245-89-2P	22246-78-2P
22246-83-9P	26416-25-1P	26670-89-3P	26673-32-5P
26902-24-9P	38968-65-9P	39554-87-5P	42984-87-2P
45121-22-0P	51219-55-7P	53346-05-7P	53842-01-6P
54043-71-9P	54147-94-3P	54656-63-2P	54752-50-0P
57521-85-4P	60656-87-3P	62517-34-4P	64113-85-5P
70680-21-6P	77234-52-7P	80253-36-7P	81445-45-6P
84358-13-4P	86499-35-6P	86499-68-5P	86499-76-5P
87268-78-8P	89711-08-0P	93742-85-9P	101043-55-4P
114772-39-3P	114772-53-1P	114772-54-2P	120519-23-5P
123226-36-8P	125993-65-9P	128182-82-1P	129765-95-3P
134174-79-1P	135689-84-8P	135689-85-9P	137036-55-6P
140700-64-7P	143654-62-0P	145457-12-1P	145457-20-1P
145457-69-8P	145457-70-1P	145485-00-3P	145485-01-4P
145485-02-5P	145485-03-6P	145485-04-7P	145485-05-8P
145485-06-9P	145485-07-0P	145485-08-1P	145485-10-5P
145485-12-7P	145485-14-9P	145485-15-0P	145485-16-1P
145485-17-2P	145485-18-3P	145485-19-4P	145485-20-7P

145485-21-8P	145485-22-9P	145485-23-0P	145485-24-1P
145485-25-2P	145485-26-3P	145485-27-4P	145485-28-5P
145485-29-6P	145485-30-9P	145485-31-0P	145485-32-1P
145485-33-2P	145485-34-3P	145485-35-4P	145485-36-5P
145485-37-6P	145485-39-8P	145485-40-1P	145485-41-2P
145485-42-3P	145485-43-4P	145485-44-5P	145485-45-6P
145485-46-7P	145485-47-8P	145485-48-9P	145485-49-0P
145485-50-3P	145485-52-5P	145485-53-6P	145485-54-7P
145485-55-8P	145485-56-9P	145485-57-0P	145485-58-1P
145485-59-2P	145485-60-5P	145485-61-6P	145485-62-7P
145485-63-8P	145485-64-9P	145485-66-1P	145485-67-2P
145485-68-3P	145485-69-4P	145485-71-8P	145485-72-9P
145485-73-0P	145485-74-1P	145485-75-2P	145485-76-3P
145485-77-4P	145485-78-5P	145485-79-6P	145485-80-9P
145485-81-0P	145485-82-1P	145485-83-2P	145485-84-3P
145485-85-4P	145485-86-5P	145485-87-6P	145485-88-7P
145485-89-8P	145485-90-1P	145485-91-2P	145485-92-3P
145485-93-4P	145485-94-5P	145485-95-6P	145485-96-7P
145485-97-8P	145485-98-9P	145485-99-0P	145486-00-6P
145486-01-7P	145486-02-8P	145486-03-9P	145486-04-0P
145486-05-1P	145486-06-2P	145486-08-4P	145486-10-8P
145486-11-9P	145486-12-0P	145486-13-1P	145486-14-2P
145486-15-3P	145486-16-4P	145486-17-5P	145486-18-6P
145486-19-7P	145486-20-0P	145486-21-1P	145486-22-2P
145486-23-3P	145486-24-4P	145486-25-5P	145486-26-6P
145486-27-7P	145486-28-8P	145486-30-2P	145486-31-3P
145486-33-5P	145486-34-6P	145486-36-8P	145486-38-0P
145486-39-1P	145486-40-4P	145486-41-5P	145486-43-7P
145486-45-9P	145486-46-0P	145486-47-1P	145486-49-3P
145486-50-6P	145486-51-7P	145486-52-8P	145486-53-9P
145486-54-0P	145486-55-1P	145486-56-2P	145486-57-3P
145486-58-4P	145486-59-5P	145486-60-8P	145486-61-9P
145486-62-0P	145486-63-1P	145486-69-7P	145486-70-0P
145486-72-2P	145486-73-3P	145486-74-4P	145486-75-5P
145554-01-4P	145554-02-5P	145554-03-6P	145554-04-7P
145554-05-8P	145554-06-9P	145554-07-0P	146429-10-9P
146429-11-0P	146429-12-1P	146429-13-2P	146429-14-3P
146429-15-4P	146429-16-5P	146429-17-6P	
146429-18-7P	146429-19-8P	146437-18-5P	
146437-19-6P	146437-20-9P	146437-21-0P	146437-22-1P
146437-23-2P			

ROLE: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as intermediate for growth hormone release promoter)

INDEX TERM:

146437-24-3P	146437-25-4P	146437-26-5P	146437-27-6P
146437-28-7P	146437-29-8P	146437-30-1P	146437-31-2P
146437-32-3P	146437-33-4P	146437-34-5P	146437-35-6P
146437-36-7P	146437-37-8P	146437-38-9P	146437-39-0P
146437-40-3P	146437-41-4P	146466-49-1P	146502-84-3P
146502-85-4P	146502-86-5P		

ROLE: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as intermediate for growth hormone release promoter)

INDEX TERM:

72-18-4, L-Valine, reactions 78-84-2 89-62-3 100-39-0
 100-46-9, Benzenemethanamine, reactions 100-47-0,
 Benzonitrile, reactions 100-52-7, Benzaldehyde, reactions
 100-79-8 103-63-9 108-59-8 109-89-7, reactions
 115-18-4 123-38-6, Propanal, reactions 141-43-5,
 reactions 306-23-0 392-83-6 455-01-6 498-94-2,
 4-Piperidinecarboxylic acid 529-34-0 557-66-4 577-19-5

597-43-3 598-32-3, 3-Buten-2-ol 611-71-2 615-36-1
 624-31-7 624-84-0, Hydrazinecarboxaldehyde 637-59-2
 676-58-4 681-57-2 687-47-8 703-67-3 921-01-7,
 D-Cysteine 1066-45-1 1078-19-9 1189-71-5, Sulfuryl
 chloride isocyanate 1489-69-6, Cyclopropanecarboxaldehyde
 1493-27-2 1667-11-4 2013-12-9, D-Norvaline 2042-37-7
 2142-69-0 2393-23-9 2483-46-7 2623-91-8 2799-16-8
 3303-84-2 3350-78-5 3976-69-0 4294-57-9 4397-53-9
 4530-20-5 5292-43-3 5470-11-1 6131-59-5 6836-19-7
 7699-00-5, Ethyl D-lactate 7745-91-7 7764-95-6
 15186-48-8 15761-38-3 17392-83-5 18942-49-9
 19914-38-6 22737-36-6 22838-58-0 26628-22-8, Sodium
 azide (Na(N3)) 27913-58-2 40353-34-2 40615-17-6
 53562-86-0 55043-49-7 56899-56-0 57294-38-9
 61228-54-4 64905-10-8 65806-90-8 69541-68-0
 75208-40-1 82732-07-8 86499-24-3 91167-29-2
 93951-18-9 114772-38-2 114772-40-6 125066-69-5
 145486-66-4 145486-67-5

ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, in preparation of growth hormone release
 promoter)

INDEX TERM: 9002-72-6, Growth hormone

ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (release promoters, benzazepinamides and related compds.)

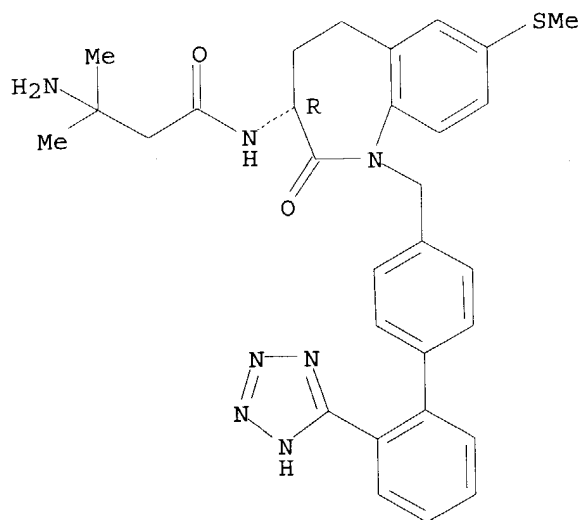
IT 145455-70-5P 145455-71-6P 145455-72-7P
 145455-73-8P 145552-97-2P 145552-98-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as growth hormone release promoter)

RN 145455-70-5 HCAPLUS

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-
 [[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-
 , (R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

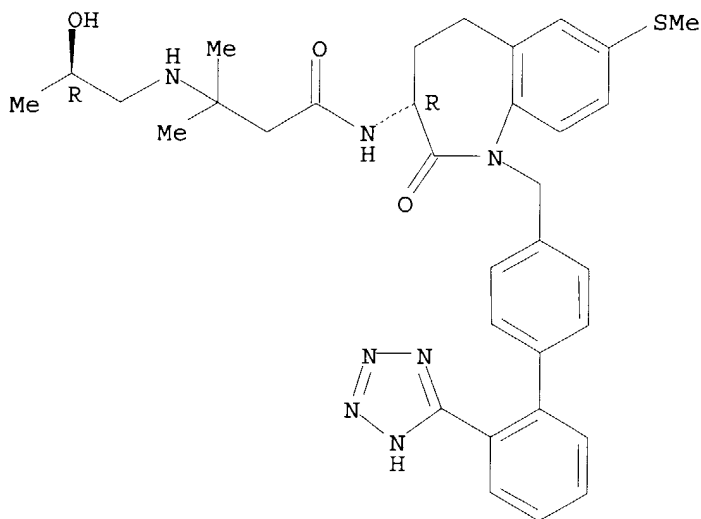


RN 145455-71-6 HCAPLUS

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-
 (methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-

1H-1-benzazepin-3-yl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

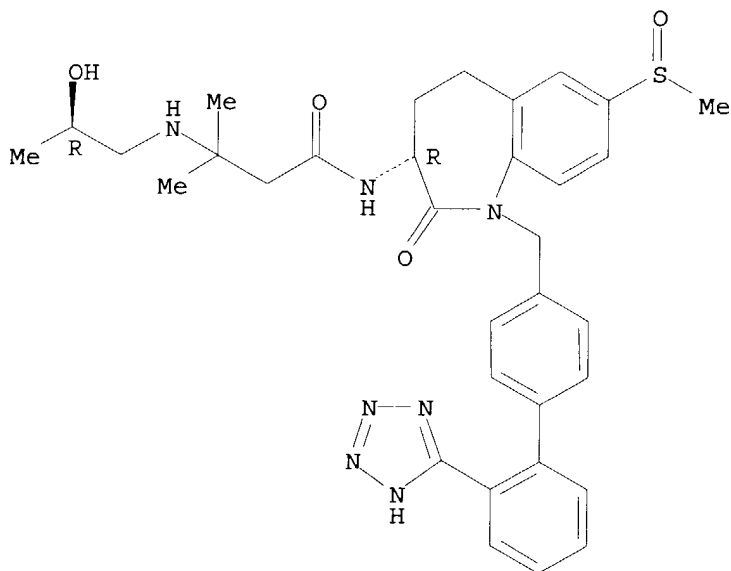
Absolute stereochemistry.



RN 145455-72-7 HCAPLUS

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, [3R-[3R*(R*)]]- (9CI) (CA INDEX NAME)

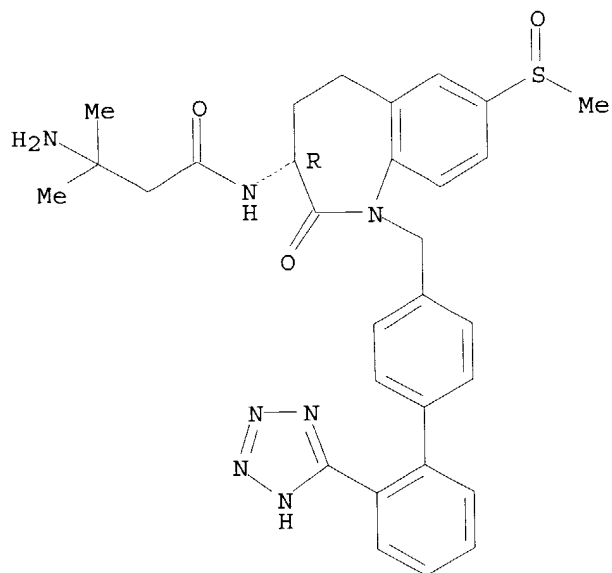
Absolute stereochemistry.



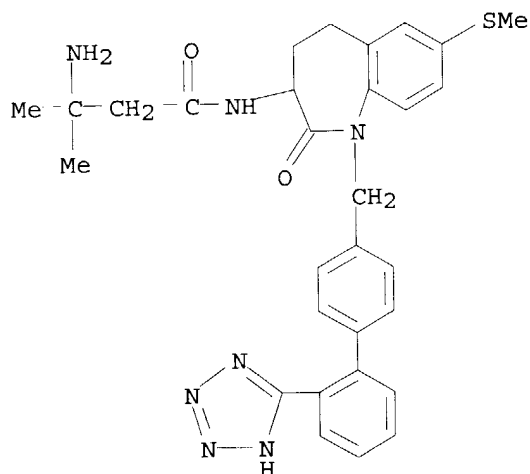
RN 145455-73-8 HCAPLUS

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfonyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

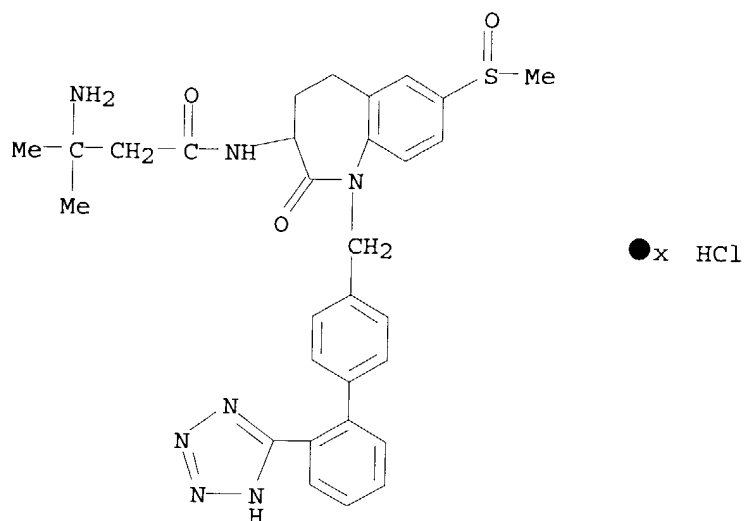


RN 145552-97-2 HCAPLUS
 CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-
 [[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-
 , hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 145552-98-3 HCAPLUS
 CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-
 oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-
 3-yl]-, hydrochloride (9CI) (CA INDEX NAME)



IT 146429-18-7P 146429-19-8P

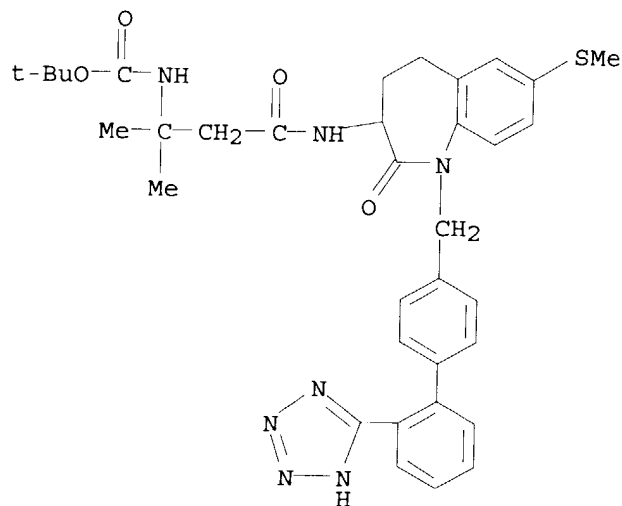
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for growth hormone release promoter)

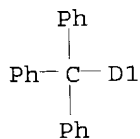
RN 146429-18-7 HCAPLUS

CN Carbamic acid, [1,1-dimethyl-3-oxo-3-[[[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-[(triphenylmethyl)-1H(or 2H)-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

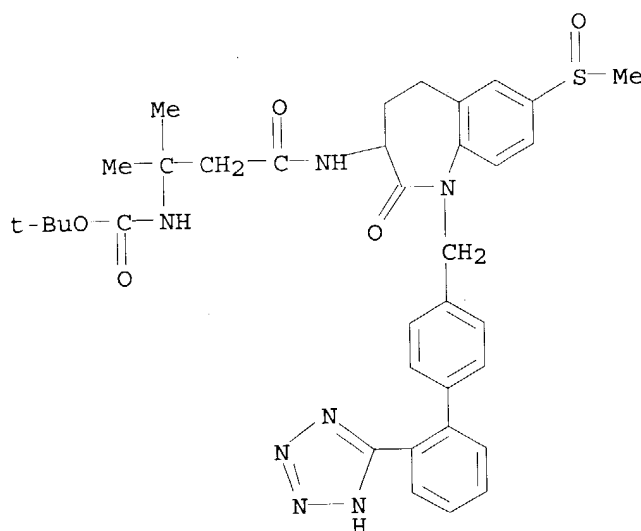


PAGE 2-A

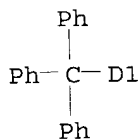


RN 146429-19-8 HCAPLUS
 CN Carbamic acid, [1,1-dimethyl-3-oxo-3-[[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-[(triphenylmethyl)-1H(or 2H)-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



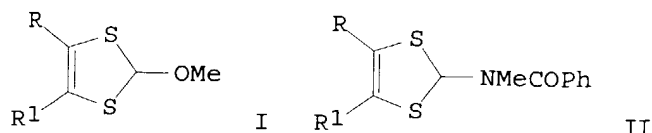
PAGE 2-A



L52 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1986:442683 HCAPLUS
 DOCUMENT NUMBER: 105:42683
 ENTRY DATE: Entered STN: 09 Aug 1986
 TITLE: Insertion of 1,3-dithiolium carbenes into the nitrogen-hydrogen bond of amides and imides
 AUTHOR(S): Buza, Daniela; Gradowska, Wanda
 CORPORATE SOURCE: Dep. Org. Chem., Polytech. Univ., Warsaw, 00664, Pol.
 SOURCE: Polish Journal of Chemistry (1984), 58(10-12), 1059-69
 CODEN: PJCHDQ; ISSN: 0137-5083
 DOCUMENT TYPE: Journal
 LANGUAGE: English

CLASSIFICATION: 28-5 (Heterocyclic Compounds (More Than One Hetero Atom))

GRAPHIC IMAGE:



ABSTRACT:

1,3-Dithiolium carbenes generated from 2-methoxy-1,3-dithioles I (R = R1 = Me, Ph; R = Ph, R1 = H; RR1 = CH:CHCH:CH) were inserted into the N-H bond of N-methylbenzamide, acetanilide, and succinimide to form N-(1,3-dithiol-2-yl)amides (imides), e.g. II, resp. N-Tosylacetamide and caprolactam were not suitable as trapping agents of the carbenes.

SUPPL. TERM: dithiolium carbene insertion amide

INDEX TERM: Carbenes (methylene derivatives)

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(dithiolium, insertion reaction of, with benzamide, diphenylacetamide, and succinimide)

INDEX TERM: Amides, reactions

Imides

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(insertion reactions of, with dithiolium carbenes)

INDEX TERM: Insertion reaction

(of dithiolium carbenes with benzamide, diphenylacetamide, and succinimide)

INDEX TERM: 24395-68-4 24395-74-2 53301-48-7 74731-83-2

ROLE: PROC (Process)

(carbene insertion of, into amides and imides)

INDEX TERM: 5152-94-3P 23780-79-2P 24648-13-3P 50708-37-7P

74731-84-3P 74731-85-4P 74731-86-5P 74731-87-6P

103214-86-4P 103214-87-5P 103214-88-6P 103214-89-7P

103214-90-0P 103214-91-1P 103214-92-2P 103214-93-3P

103214-94-4P **103214-95-5P 103214-96-6P**

103214-97-7P

ROLE: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

INDEX TERM: 23780-83-8 24396-11-0 32283-21-9 50708-36-6

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with caprolactam)

INDEX TERM: 37912-62-2 103214-98-8

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with diphenyldithiolium perchlorate)

INDEX TERM: 103-84-4 123-56-8 613-93-4

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with dithiolium carbenes)

INDEX TERM: 105-60-2, reactions

ROLE: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with methoxydithioles in presence of trichloroacetic acid and dithiolium perchlorates)

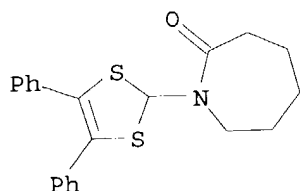
IT **103214-95-5P 103214-96-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)

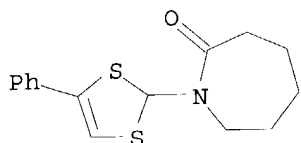
(preparation of)

RN 103214-95-5 HCAPLUS

CN 2H-Azepin-2-one, 1-(4,5-diphenyl-1,3-dithiol-2-yl)hexahydro- (9CI) (CA
INDEX NAME)



RN 103214-96-6 HCAPLUS
CN 2H-Azepin-2-one, hexahydro-1-(4-phenyl-1,3-dithiol-2-yl)- (9CI) (CA INDEX
NAME)



=> d ibib abs ed hitstr 17

'ED' IS NOT A VALID FORMAT

In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.

REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ibib abs hitstr

L52 ANSWER 17 OF 27 USPATFULL on STN

ACCESSION NUMBER: 2003:238768 USPATFULL

TITLE: Pyrroloazepine derivatives

INVENTOR(S): Mizuno, Akira, Kyoto-shi, JAPAN

Shibata, Makoto, Ashikaga-shi, JAPAN

Iwamori, Tomoe, Ibaraki-shi, JAPAN

Shimamoto, Tetsuo, Suita-shi, JAPAN

Nakanishi, Kyoko, Ibaraki-shi, JAPAN

Inomata, Norio, Minoo-shi, JAPAN

PATENT ASSIGNEE(S): SUNTORY LIMITED, Osaka-shi, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003166926	A1	20030904
	US 6713634	B2	20040330
APPLICATION INFO.:	US 2002-188234	A1	20020703 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-801816, filed on 9 Mar 2001, GRANTED, Pat. No. US 6489473		
	Continuation of Ser. No. US 1999-312713, filed on 17 May 1999, GRANTED, Pat. No. US 6258805		
	Continuation of Ser. No. US 1997-875495, filed on 21 Aug 1997, GRANTED, Pat. No. US 5962448 A		
	371 of International Ser. No. WO 1996-JP3522, filed on 2 Dec 1996, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1995-335714	19951201
	JP 1996-46928	19960209
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202	
NUMBER OF CLAIMS:	39	
EXEMPLARY CLAIM:	1	
LINE COUNT:	4287	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of effecting serotonin-2-receptor antagonism in a mammal in need thereof, which includes administering to the mammal an effective amount of the compound of the formula (I), or a pharmaceutically acceptable salt thereof: ##STR1##

wherein ring P, the dashed line, A, Y, Z.sub.1 and Z.sub.2 are defined herein.

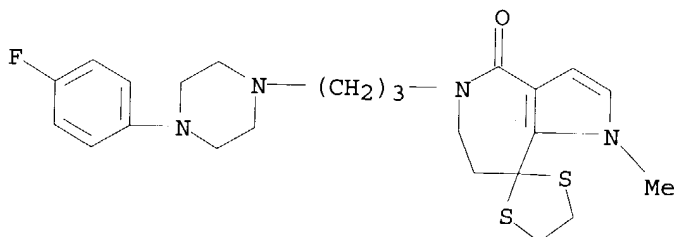
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 191592-05-9p

(preparation of pyrroloazepine derivs. as serotonin-2 receptor antagonists)

RN 191592-05-9 USPATFULL

CN Spiro[1,3-dithiolane-2,8'-(1'H)-pyrrolo[3,2-c]azepin]-4'-(5'H)-one, 5'-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-6',7'-dihydro-1'-methyl- (9CI) (CA INDEX NAME)



=> d ibib abs hitstr 18-

YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L52 ANSWER 18 OF 27 USPATFULL on STN

ACCESSION NUMBER: 2002:141528 USPATFULL

TITLE: Pyrroloazepine derivatives

INVENTOR(S): Mizuno, Akira, Kyoto-shi, JAPAN

Shibata, Makoto, Ashikaga-shi, JAPAN

Iwamori, Tomoe, Ibaraki-shi, JAPAN

Shimamoto, Tetsuo, Suita-shi, JAPAN

Nakanishi, Kyoko, Ibaraki-shi, JAPAN

Inomata, Norio, Minoo-shi, JAPAN

PATENT ASSIGNEE(S): SUNTORY LIMITED, Osaka-shi, JAPAN, 530 (non-U.S. corporation)

NUMBER	KIND	DATE
--------	------	------

PATENT INFORMATION: US 2002072515 A1 20020613
 US 6489473 B2 20021203
 APPLICATION INFO.: US 2001-801816 A1 20010309 (9)
 RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-312713, filed on 17
 May 1999, GRANTED, Pat. No. US 6258805 Continuation of
 Ser. No. US 1997-875495, filed on 21 Aug 1997, GRANTED,
 Pat. No. US 5962448 Continuation of Ser. No. WO
 1996-JP3522, filed on 2 Dec 1996, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1995-335714	19951201
	JP 1996-46928	19960209
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202	
NUMBER OF CLAIMS:	39	
EXEMPLARY CLAIM:	1	
LINE COUNT:	4156	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of effecting serotonin-2-receptor antagonism in a mammal in
 need thereof, which entails administering to the mammal an effective
 amount of a compound of the formula (I), or a pharmaceutically
 acceptable salt thereof: ##STR1##

wherein ring P, the dashed line, Z.sub.1, Z.sub.2, A and Y are as
 defined herein.

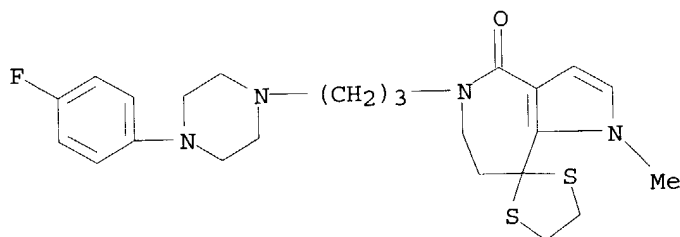
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 191592-05-9P

(preparation of pyrroloazepine derivs. as serotonin-2 receptor antagonists)

RN 191592-05-9 USPATFULL

CN Spiro[1,3-dithiolane-2,8'-(1'H)-pyrrolo[3,2-c]azepin]-4'-(5'H)-one,
 5'-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-6',7'-dihydro-1'-methyl-
 (9CI) (CA INDEX NAME)



L52 ANSWER 19 OF 27 USPATFULL on STN

ACCESSION NUMBER: 1999:121350 USPATFULL

TITLE: Pyrroloazepine derivatives

INVENTOR(S): Mizuno, Akira, Kyoto, Japan

Shibata, Makoto, Ashikaga, Japan

Iwamori, Tomoe, Ibaraki, Japan

Shimamoto, Tetsuo, Suita, Japan

Nakanishi, Kyoko, Ibaraki, Japan

Inomata, Norio, Minoo, Japan

PATENT ASSIGNEE(S): Suntory Limited, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5962448		19991005
	WO 9720845		19970612
APPLICATION INFO.:	US 1997-875495		19970821 (8)
	WO 1996-JP3522		19961202
			19970821 PCT 371 date
			19970821 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1995-335714	19951201
	JP 1996-46928	19960209
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Shah, Mukund J.	
ASSISTANT EXAMINER:	Kifle, Bruck	
LEGAL REPRESENTATIVE:	Oblon, Spivak, McClelland, Maier & Neustadt, P.C.	
NUMBER OF CLAIMS:	31	
EXEMPLARY CLAIM:	1	
LINE COUNT:	4644	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pyrroloazepine compound having the following formula (I): wherein

the ring P represented by ##STR1## is a pyrrole ring having the following structure: ##STR2## wherein R.sub.1 represents C.sub.1 -C.sub.8 alkyl, C.sub.3 -C.sub.8 cycloalkyl, C.sub.4 -C.sub.8 cycloalkyl-alkyl, C.sub.6 -C.sub.14 aryl or C.sub.7 -C.sub.22 aralkyl, which are optionally substituted; and R.sub.2 represents H or C.sub.1 -C.sub.8 alkyl, which is optionally substituted; the dashed line indicates the presence or absence of a bond; and, when the bond is present, Z.sub.2 is not present and Z.sub.1 represents H, but, when the bond is absent, Z.sub.1 and Z.sub.2 are both H; Z.sub.1 represents H and Z.sub.2 represents a group OR.sub.3, in which R.sub.3 represents H, C.sub.1 -C.sub.8 alkyl, or C.sub.7 -C.sub.22 aralkyl, which are optionally substituted; Z.sub.1 and Z.sub.2 both represent groups SR.sub.4, in which R.sub.4 represents C.sub.1 -C.sub.8 alkyl or C.sub.7 -C.sub.22 aralkyl, which are optionally substituted; or Z.sub.1 and Z.sub.2 are combined together to represent O, a group NOR.sub.5, in which R.sub.5 represents H, or C.sub.1 -C.sub.8 alkyl or C.sub.2 -C.sub.3 alkylenedithio, which are optionally substituted; A represents alkylene, alkenylene or alkenylene; and Y represents a group in which W is CH, C.dbd. or N, m is for 0 or 1, n is for 1, 2 or 3, G is O, S, C.dbd.O, sulfinyl, sulfonyl, alkylene, alkenylene or acetal; E.sub.1 and E.sub.2 is H or C.sub.1 -C.sub.8 alkyl; and D represents an aromatic hydrocarbon or an aromatic heterocyclic ring. The compound (I) has strong serotonin-2 receptor antagonistic action and low toxicity and less side effects, and is therapeutically useful in the treatment of circulatory diseases and/or conditions related thereto.

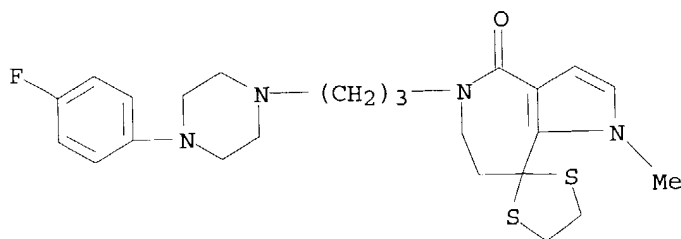
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 191592-05-9P

(preparation of pyrroloazepine derivs. as serotonin-2 receptor antagonists)

RN 191592-05-9 USPATFULL

CN Spiro[1,3-dithiolane-2,8'-(1'H)-pyrrolo[3,2-c]azepin]-4'-(5'H)-one,
5'-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-6',7'-dihydro-1'-methyl-
(9CI) (CA INDEX NAME)



L52 ANSWER 20 OF 27 USPTAFULL on STN
 ACCESSION NUMBER: 1998:25360 USPTAFULL
 TITLE: Benzo-fused lactams promote release of growth hormone
 INVENTOR(S): Schoen, William R., Edison, NJ, United States
 Wyvratt, Matthew J., Mountainside, NJ, United States
 PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5726307		19980310
APPLICATION INFO.:	US 1994-356935		19941215 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1992-961008, filed on 14 Oct 1992, now patented, Pat. No. US 5374721, issued on 20 Dec 1994		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Bond, Robert T.		
LEGAL REPRESENTATIVE:	Thies, J. Eric, Rose, David L.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2191		

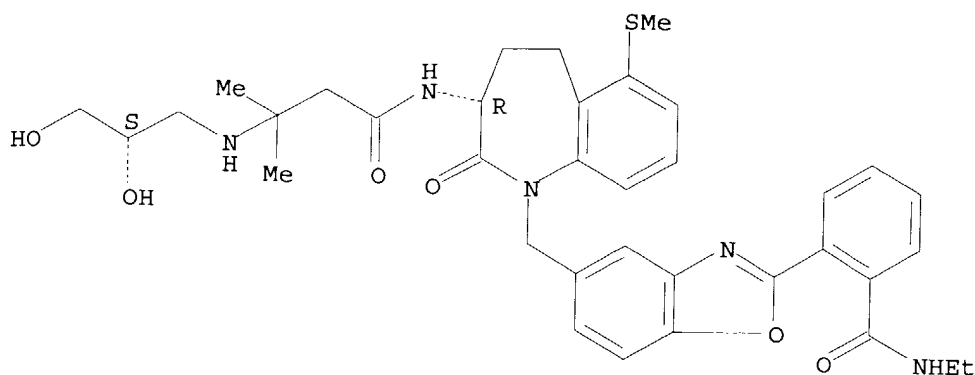
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain novel compounds identified as benzo-fused lactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzo-fused lactams as the active ingredient thereof are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

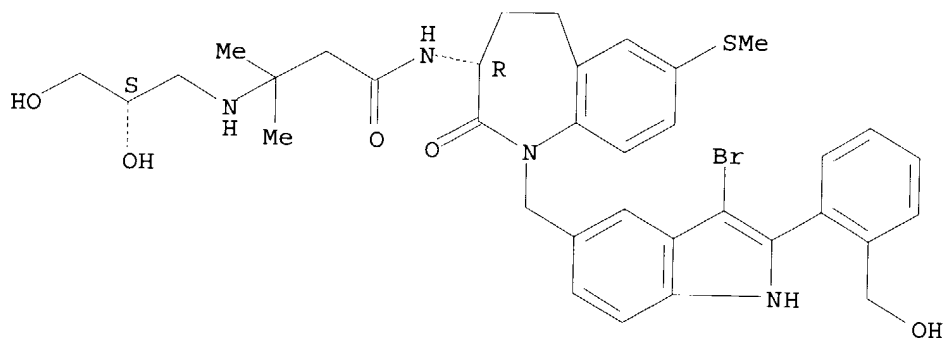
IT **167822-74-4P 167822-97-1P**
 (preparation of N-(N-heterocyclylbenzazepinyl)aminoalkanamides as growth hormone release promoters)
 RN 167822-74-4 USPTAFULL
 CN Benzamide, 2-[5-[[3-[[3-[(2,3-dihydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-6-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl]-2-benzoxazolyl]-N-ethyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 167822-97-1 USPATFULL
 CN Butanamide, N-[1-[[3-bromo-2-[2-(hydroxymethyl)phenyl]-1H-indol-5-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2,3-dihydroxypropyl)amino]-3-methyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L52 ANSWER 21 OF 27 USPATFULL on STN
 ACCESSION NUMBER: 96:72979 USPATFULL
 TITLE: Benzo-Fused Lactams promote release of growth hormone
 INVENTOR(S): Bochis, Richard J., East Brunswick, NJ, United States
 Hodges, Paul J., Brick, NJ, United States
 Schoen, William R., Edison, NJ, United States
 Wyvratt, Jr., Matthew J., Mountainside, NJ, United States
 PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5545735		19960813
APPLICATION INFO.:	US 1993-132074		19931004 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Ford, John M.		
LEGAL REPRESENTATIVE:	Thies, Eric J., Rose, David L.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		

LINE COUNT: 3239
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain novel compounds identified as benzo-fused lactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzo-fused lactams as the active ingredient thereof are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

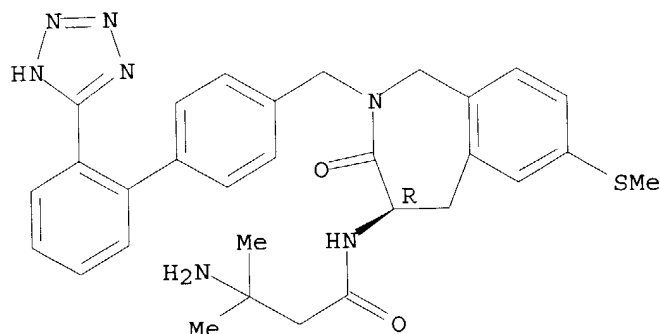
IT 168057-13-4P 168057-14-5P 168057-15-6P
168057-16-7P 168057-25-8P 168057-26-9P
168057-27-0P 168057-37-2P 168057-45-2P
168057-46-3P 168057-47-4P 168057-55-4P
168057-61-2P 168057-67-8P 168057-69-0P
168057-72-5P 168057-78-1P 168057-84-9P
168057-88-3P 168057-92-9P 168057-96-3P
168058-00-2P 168058-04-6P

(preparation of N-(benzazepinonyl)alkanamides as growth hormone release promoters)

RN 168057-13-4 USPTAFULL

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-2-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

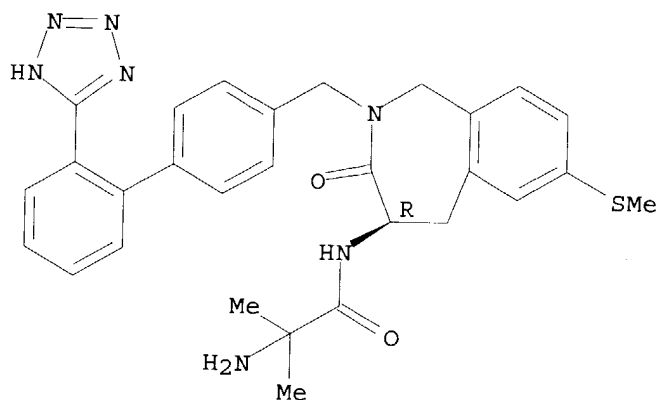
Absolute stereochemistry.



RN 168057-14-5 USPTAFULL

CN Propanamide, 2-amino-2-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-2-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

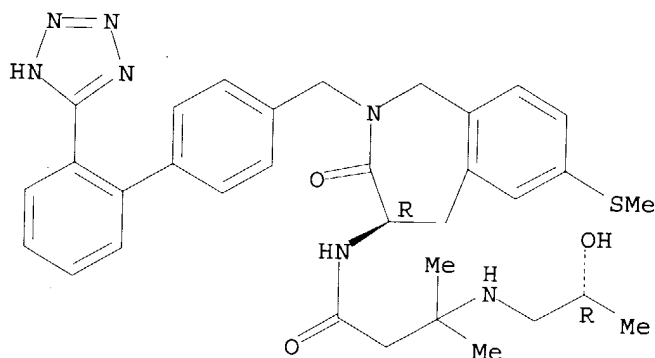
Absolute stereochemistry.



RN 168057-15-6 USPATFULL

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-2-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-2-benzazepin-4-yl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

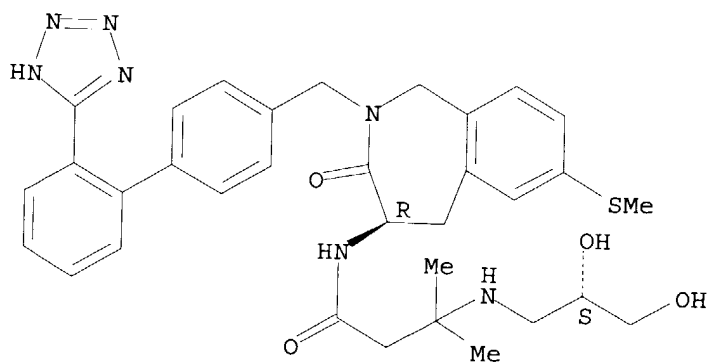
Absolute stereochemistry.



RN 168057-16-7 USPATFULL

CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-2-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-2-benzazepin-4-yl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

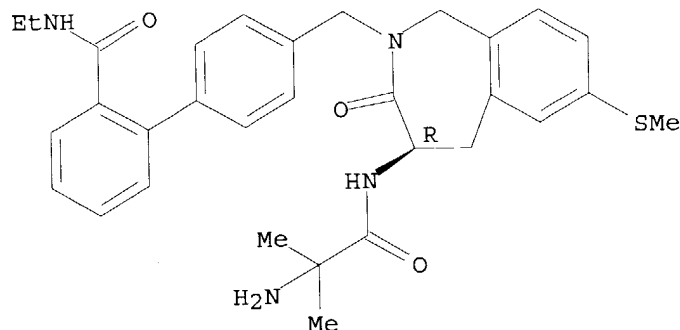
Absolute stereochemistry.



RN 168057-25-8 USPATFULL

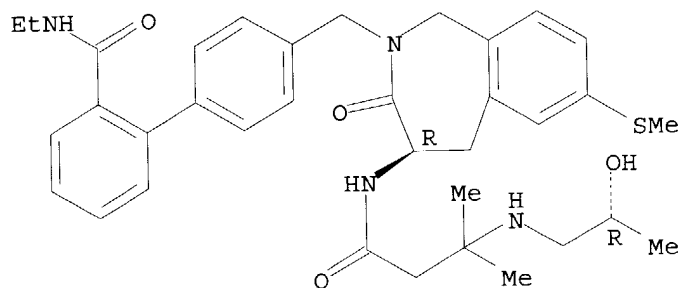
CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[4-[(2-amino-2-methyl-1-oxopropyl)amino]-1,3,4,5-tetrahydro-7-(methylthio)-3-oxo-2H-2-benzazepin-2-yl]methyl]-N-ethyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



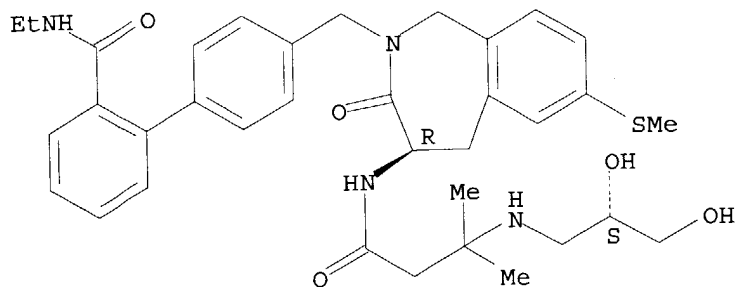
RN 168057-26-9 USPATFULL
CN [1,1'-Biphenyl]-2-carboxamide, N-ethyl-4'-[[1,3,4,5-tetrahydro-4-[[3-[(2-hydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-7-(methylthio)-3-oxo-2H-2-benzazepin-2-yl]methyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168057-27-0 USPATFULL
CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[4-[[3-[(2,3-dihydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-1,3,4,5-tetrahydro-7-(methylthio)-3-oxo-2H-2-benzazepin-2-yl]methyl]-N-ethyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

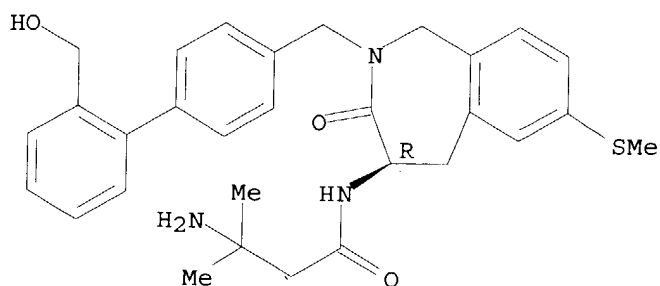
Absolute stereochemistry.



RN 168057-37-2 USPATFULL
CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-

(hydroxymethyl) [1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

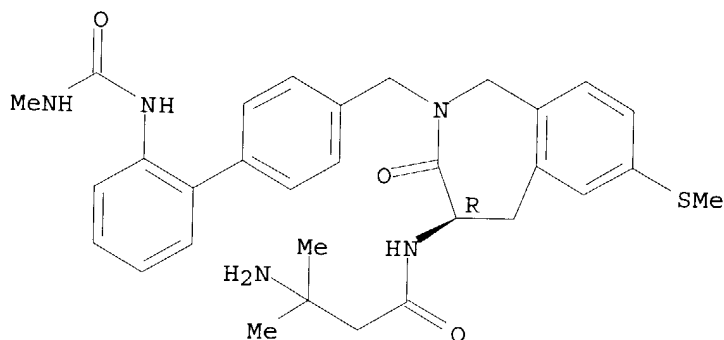
Absolute stereochemistry.



RN 168057-45-2 USPATFULL

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(methylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

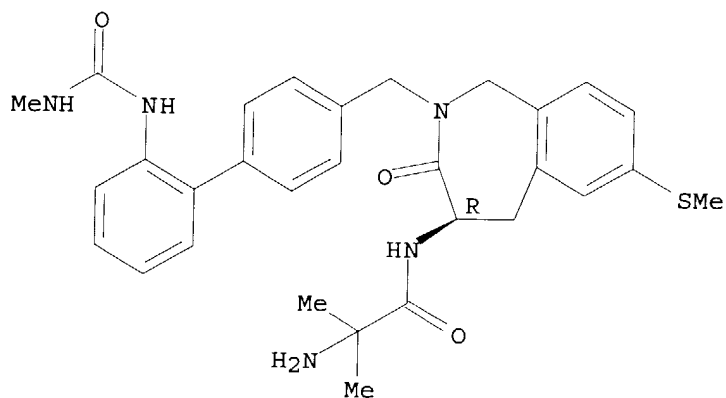
Absolute stereochemistry.



RN 168057-46-3 USPATFULL

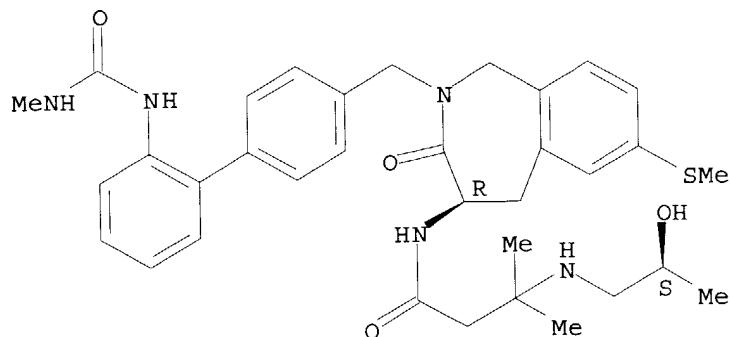
CN Propanamide, 2-amino-2-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(methylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



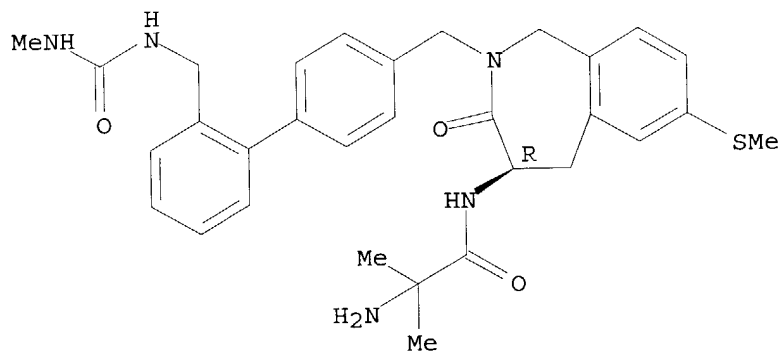
RN 168057-47-4 USPATFULL
 CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-
 [[2'-[[[(methylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]methyl]-7-
 (methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, [S-(R*,S*)]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.



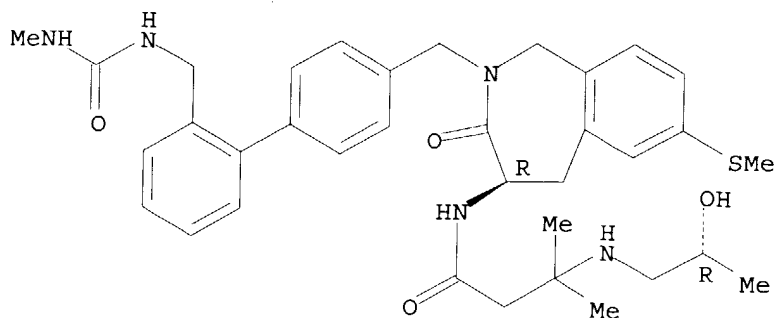
RN 168057-55-4 USPATFULL
 CN Propanamide, 2-amino-2-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-
 [[[(methylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-
 (methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168057-61-2 USPATFULL
 CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-
 [[2'-[[[(methylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-
 (methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, [R-(R*,R*)]- (9CI) (CA
 INDEX NAME)

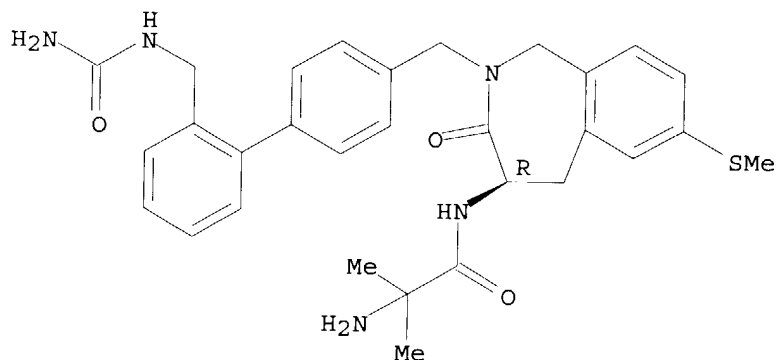
Absolute stereochemistry.



RN 168057-67-8 USPATFULL

CN Propanamide, 2-amino-N-[2-[[2'-[[[(aminocarbonyl)amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

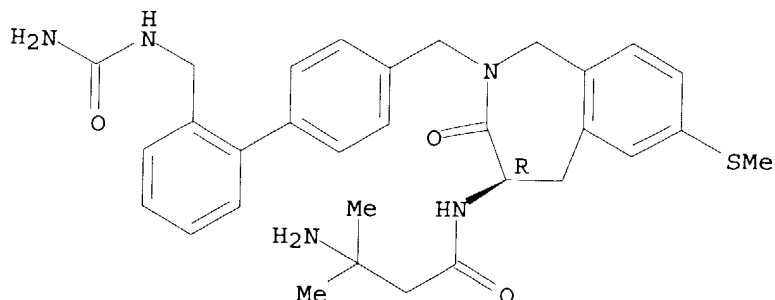
Absolute stereochemistry.



RN 168057-69-0 USPATFULL

CN Butanamide, 3-amino-N-[2-[[2'-[[[(aminocarbonyl)amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

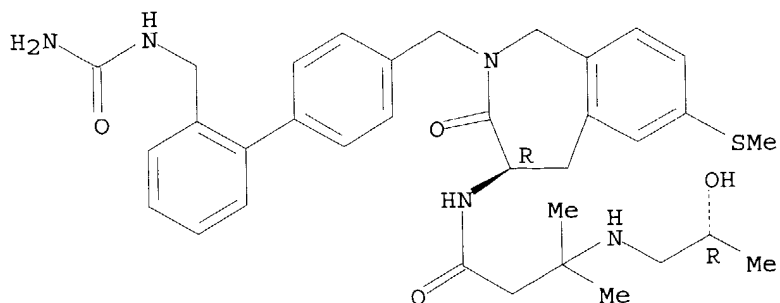


RN 168057-72-5 USPATFULL

CN Butanamide, N-[2-[[2'-[[[(aminocarbonyl)amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

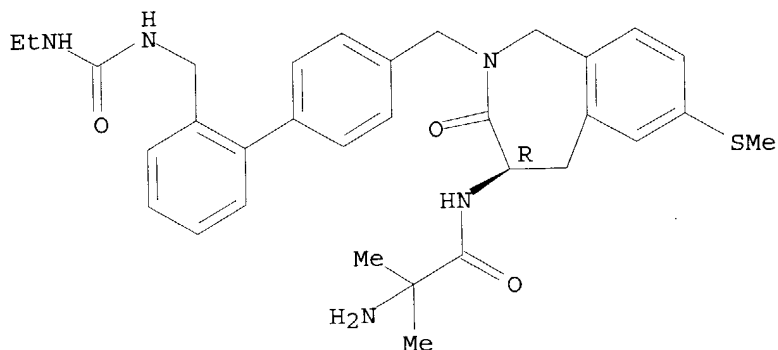
NAME)

Absolute stereochemistry.



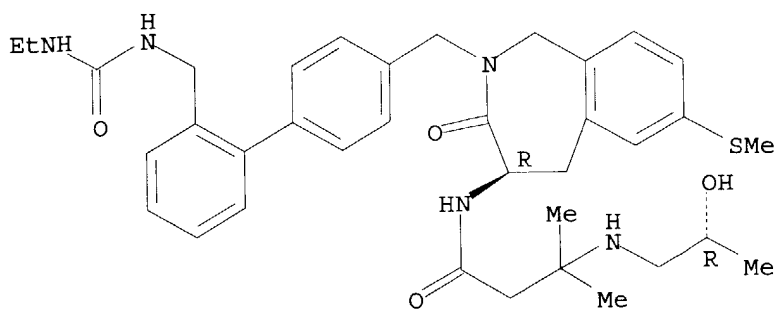
RN 168057-78-1 USPATFULL
 CN Propanamide, 2-amino-N-[2-[[2'-[[[(ethylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168057-84-9 USPATFULL
 CN Butanamide, N-[2-[[2'-[[[(ethylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

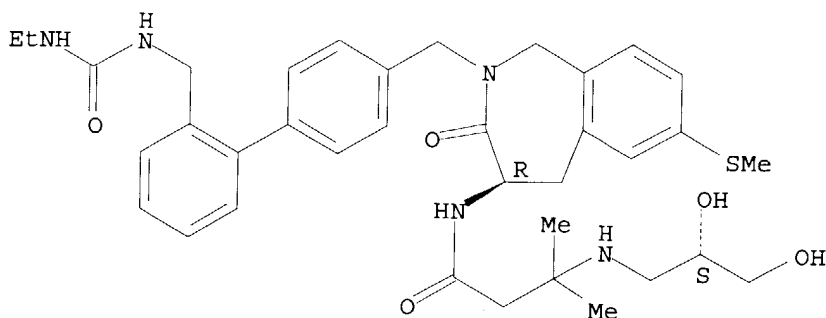
Absolute stereochemistry.



RN 168057-88-3 USPATFULL

CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-N-[2-[[2'-
 [[[ethylamino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-
 2,3,4,5-tetrahydro-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-3-methyl-,
 [S-(R*,S*)]-(9CI) (CA INDEX NAME)

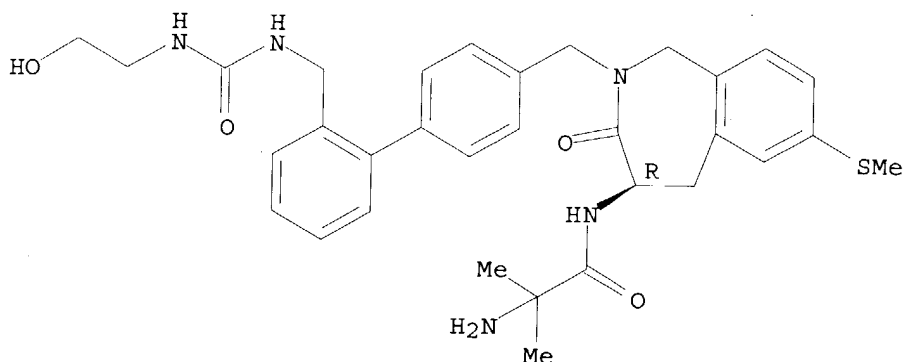
Absolute stereochemistry.



RN 168057-92-9 USPATFULL

CN Propanamide, 2-amino-2-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)-(9CI) (CA INDEX NAME)

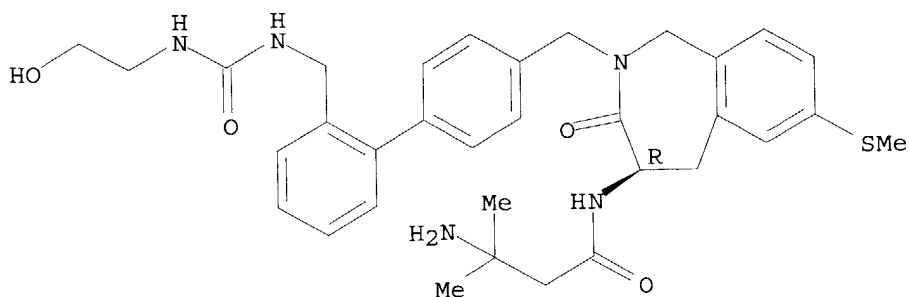
Absolute stereochemistry.



RN 168057-96-3 USPATFULL

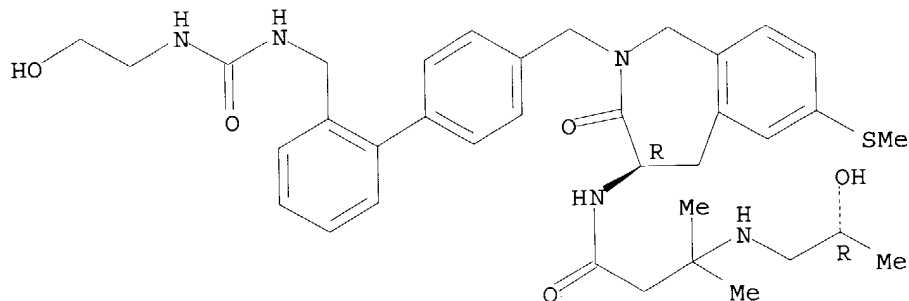
CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



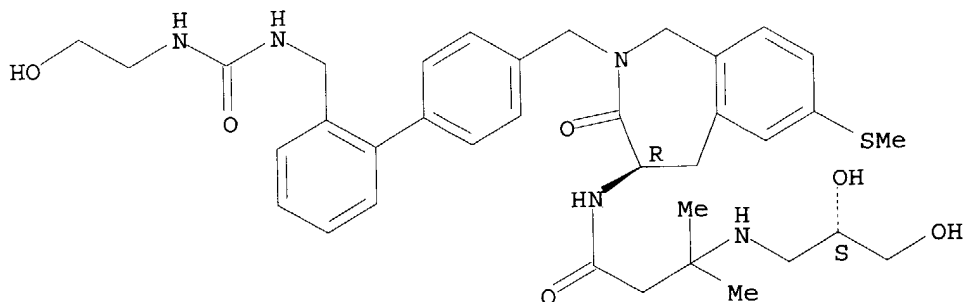
RN 168058-00-2 USPATFULL
 CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, [R-(R*,R*)]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 168058-04-6 USPATFULL
 CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-[[2'-[[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-3-oxo-1H-2-benzazepin-4-yl]-, [R-(R*,S*)]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L52 ANSWER 22 OF 27 USPATFULL on STN
 ACCESSION NUMBER: 95:65030 USPATFULL
 TITLE: Benzo-fused lactams promote release of growth hormone

INVENTOR(S): Schoen, William R., Edison, NJ, United States
 Wyvratt, Jr., Matthew J., Mountainside, NJ, United States
 PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5434261		19950718
APPLICATION INFO.:	US 1993-97149		19930726 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Bond, Robert T.		
LEGAL REPRESENTATIVE:	Thies, J. Eric, Rose, David L.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2342		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain novel compounds identified as benzo-fused lactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzo-fused lactams as the active ingredient thereof are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

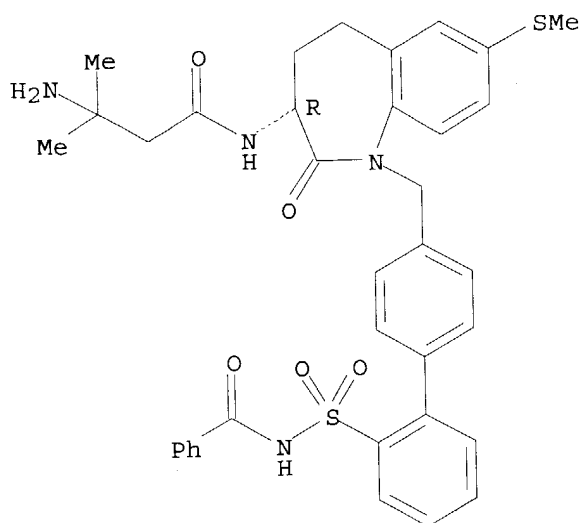
IT 169188-22-1P 169188-27-6P 169188-32-3P
 169188-37-8P 169188-42-5P 169188-47-0P
 169188-52-7P 169188-57-2P 169188-61-8P
 169188-66-3P 169188-71-0P 169188-76-5P
 169188-80-1P 169188-85-6P 169188-90-3P
 169188-95-8P

(preparation of benzo-fused lactams which promote release of growth hormone)

RN 169188-22-1 USPATFULL

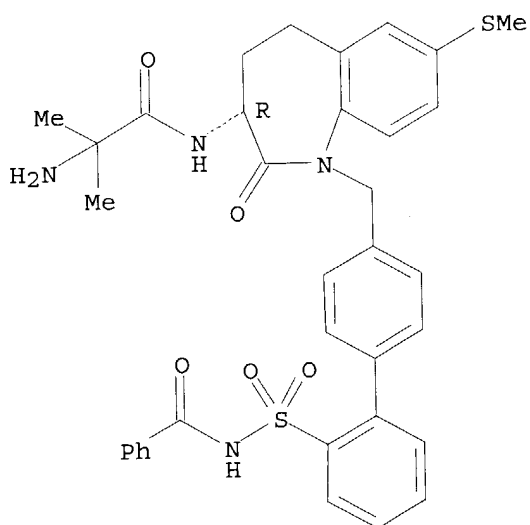
CN Benzamide, N-[[4'-[[3-[(3-amino-3-methyl-1-oxobutyl)amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



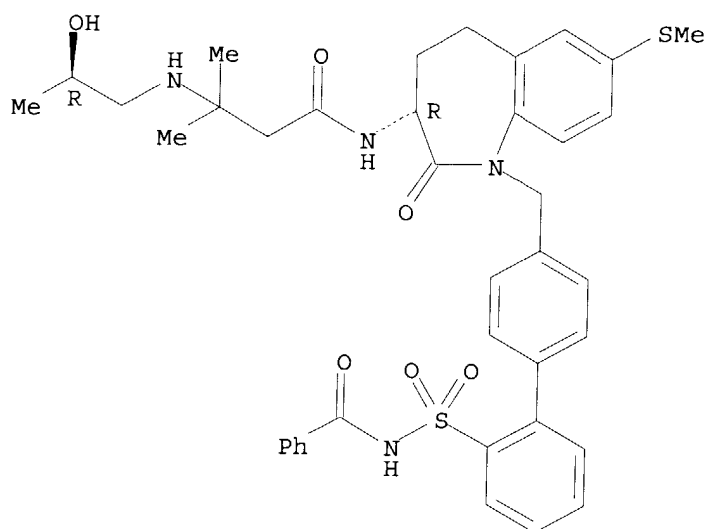
RN 169188-27-6 USPATFULL
 CN Benzamide, N-[[4'-[[3'-[(2-amino-2-methyl-1-oxopropyl)amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169188-32-3 USPATFULL
 CN Benzamide, N-[[4'-[[2,3,4,5-tetrahydro-3-[[3'-[(2-hydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

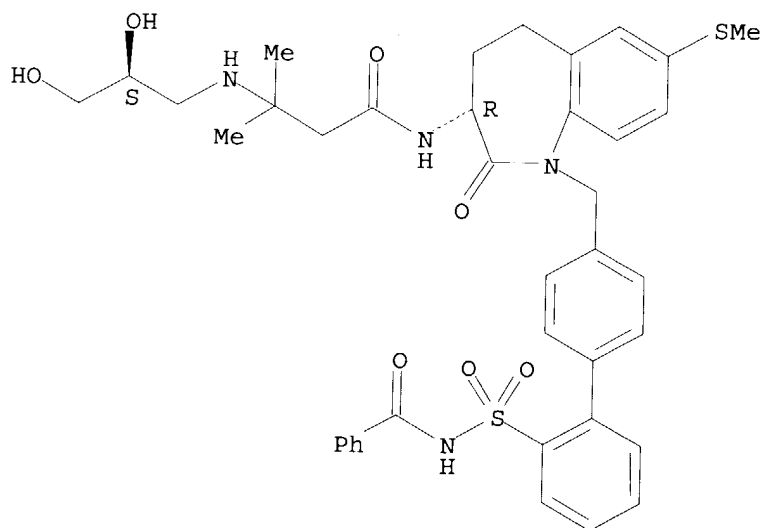
Absolute stereochemistry.



RN 169188-37-8 USPATFULL

CN Benzamide, N-[[4'-[[3-[[3-[(2,3-dihydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl][1,1'-biphenyl]-2-yl]sulfonyl]-, [S-(R*,S*)]-(9CI) (CA INDEX NAME)

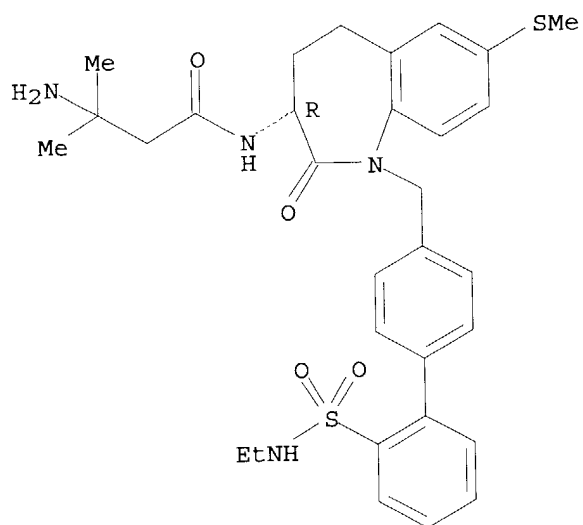
Absolute stereochemistry.



RN 169188-42-5 USPATFULL

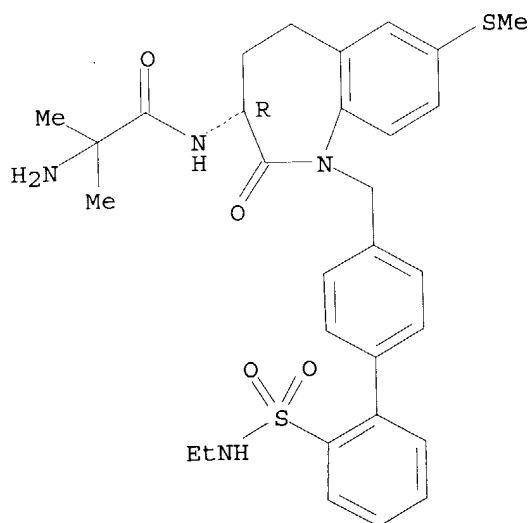
CN Butanamide, 3-amino-N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



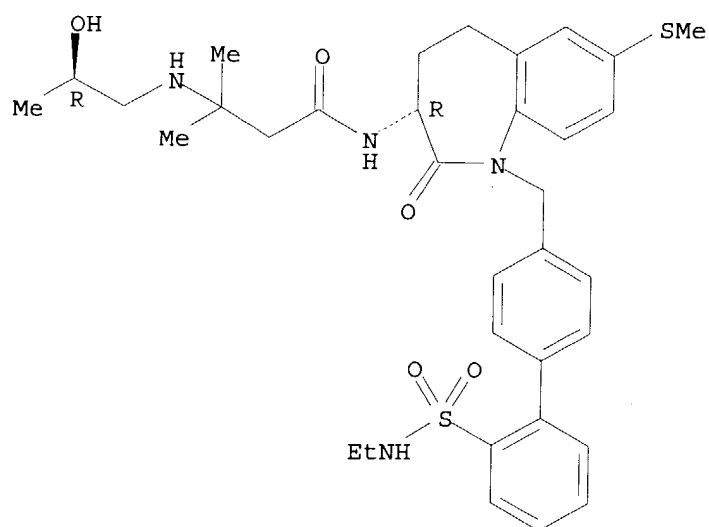
RN 169188-47-0 USPATFULL
 CN Propanamide, 2-amino-N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



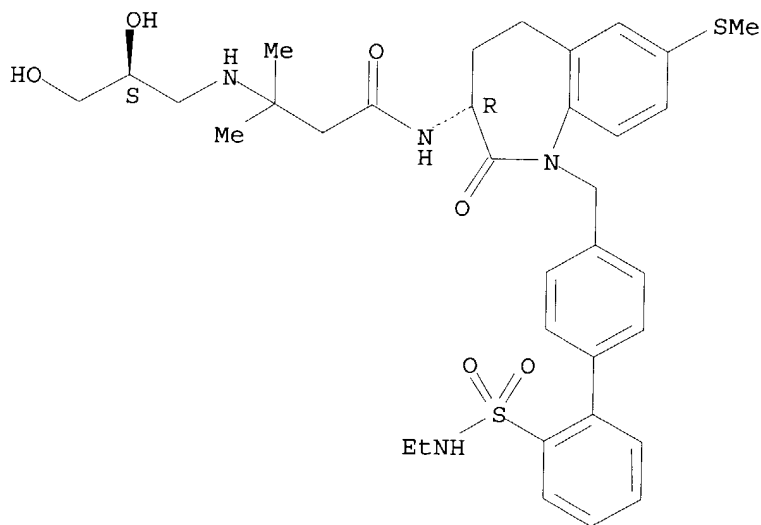
RN 169188-52-7 USPATFULL
 CN Butanamide, N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



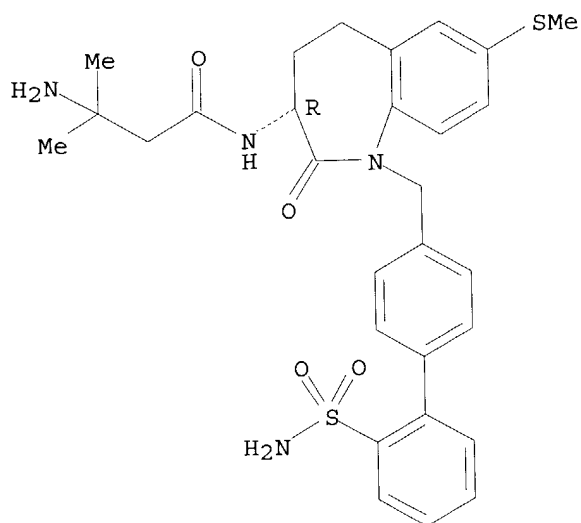
RN 169188-57-2 USPATFULL
 CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-N-[1-[[2'-[(ethylamino)sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, [S-(R*,S*)]]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



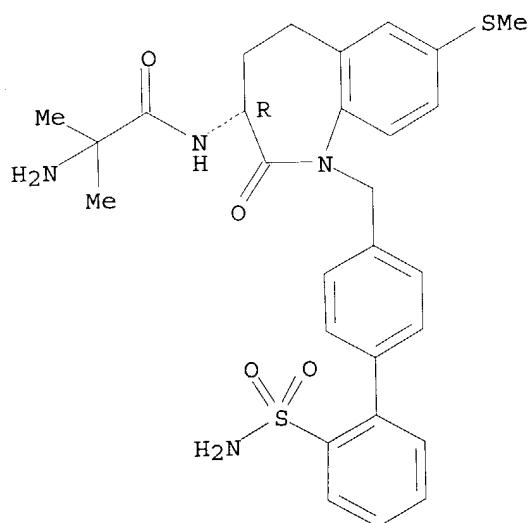
RN 169188-61-8 USPATFULL
 CN Butanamide, 3-amino-N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



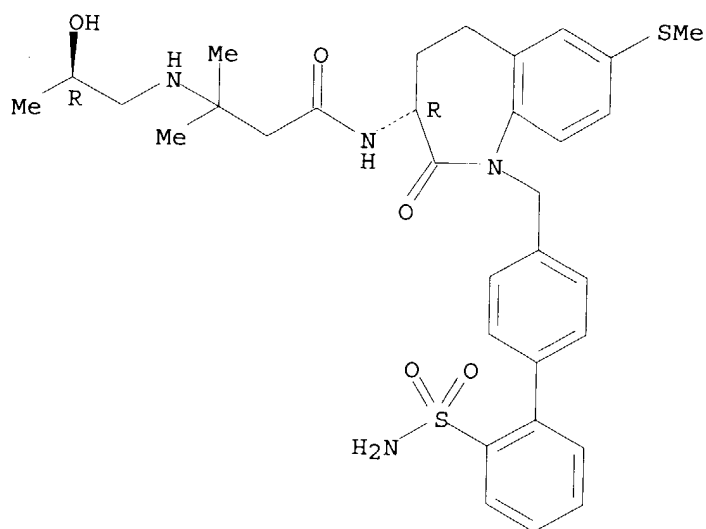
RN 169188-66-3 USPATFULL
 CN Propanamide, 2-amino-N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169188-71-0 USPATFULL
 CN Butanamide, N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

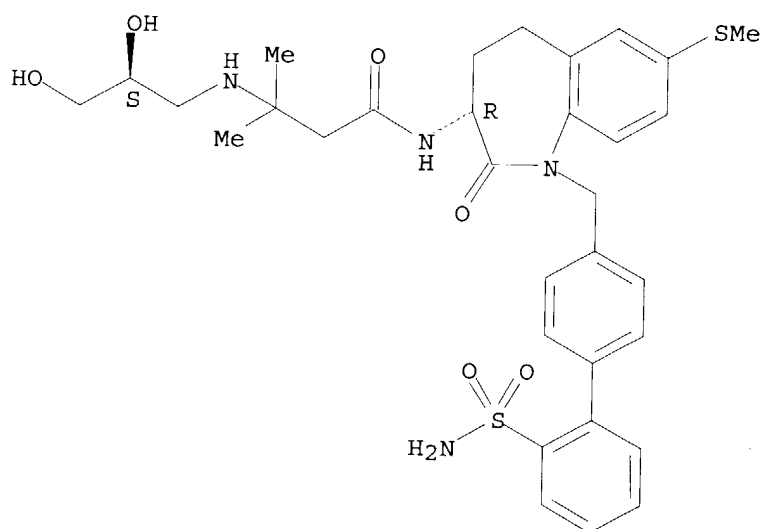
Absolute stereochemistry.



RN 169188-76-5 USPATFULL

CN Butanamide, N-[1-[[2'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2,3-dihydroxypropyl)amino]-3-methyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

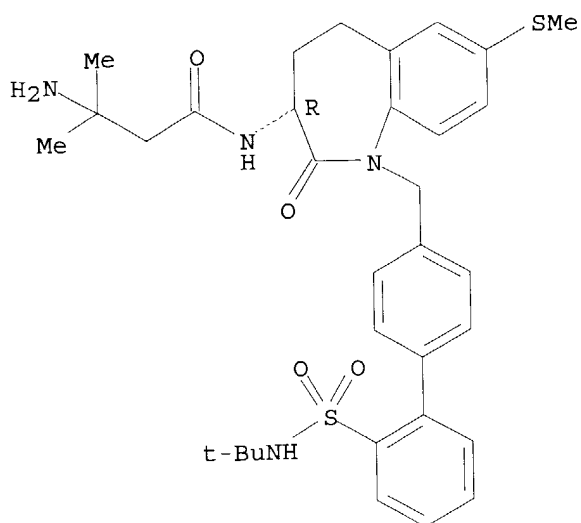
Absolute stereochemistry.



RN 169188-80-1 USPATFULL

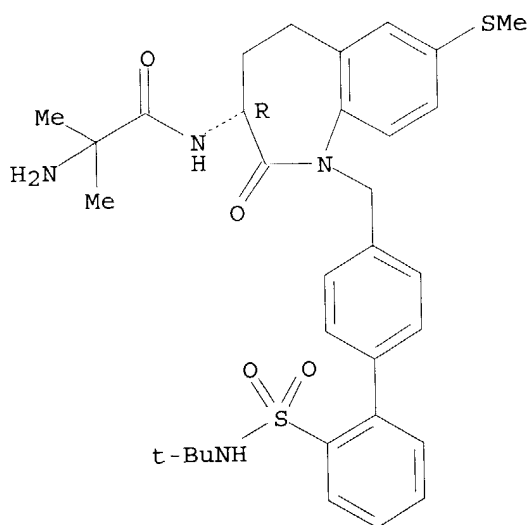
CN Butanamide, 3-amino-N-[1-[[2'-[[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



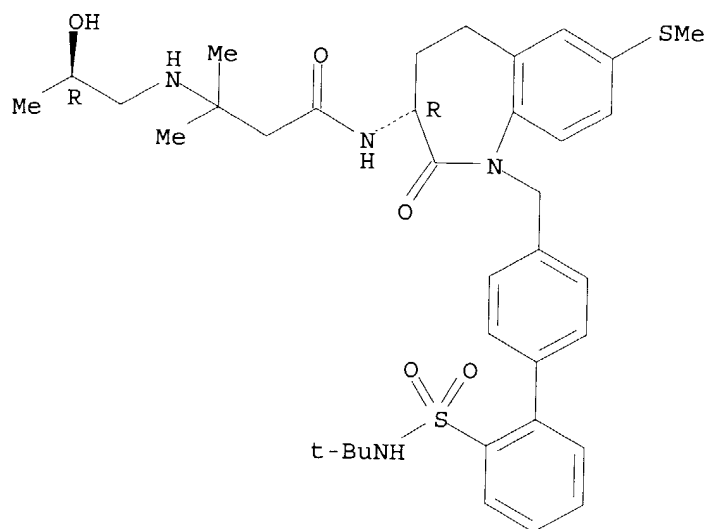
RN 169188-85-6 USPATFULL
 CN Propanamide, 2-amino-N-[1-[[2'-[[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169188-90-3 USPATFULL
 CN Butanamide, N-[1-[[2'-[[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-hydroxypropyl)amino]-3-methyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

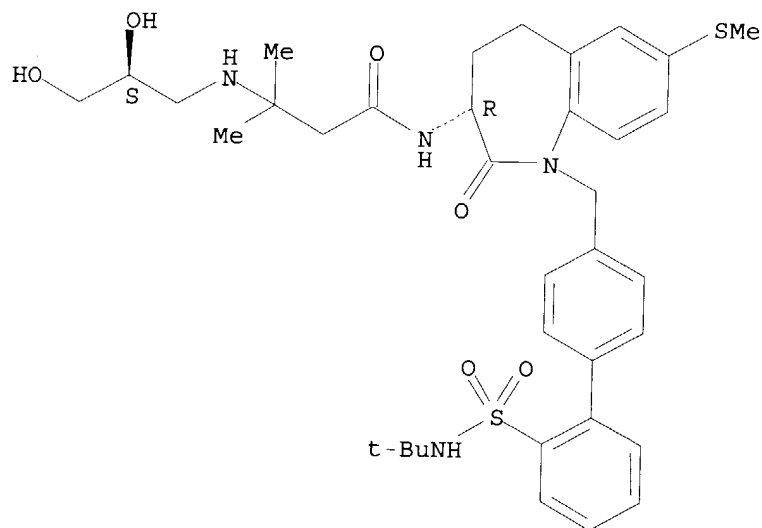
Absolute stereochemistry.



RN 169188-95-8 USPATFULL

CN Butanamide, 3-[(2,3-dihydroxypropyl)amino]-N-[1-[[2'-[[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-methyl-, [S-(R*,S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L52 ANSWER 23 OF 27 USPATFULL on STN

ACCESSION NUMBER: 95:60479 USPATFULL

TITLE: Benzo-fused lactams promote release of growth hormone

INVENTOR(S): Schoen, William R., Edison, NJ, United States
Wyvratt, Jr., Matthew J., Mountainside, NJ, United States

PATENT ASSIGNEE(S): Hodges, Paul J., Brick, NJ, United States
Merck & Co., Inc., Rahway, NJ, United States (U.S.)

corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5430144		19950704
APPLICATION INFO.:	US 1993-97146		19930726 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Bond, Robert T.		
LEGAL REPRESENTATIVE:	Thies, J. Eric, Rose, David		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2326		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain novel compounds identified as benzo-fused lactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzo-fused lactams as the active ingredient thereof are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

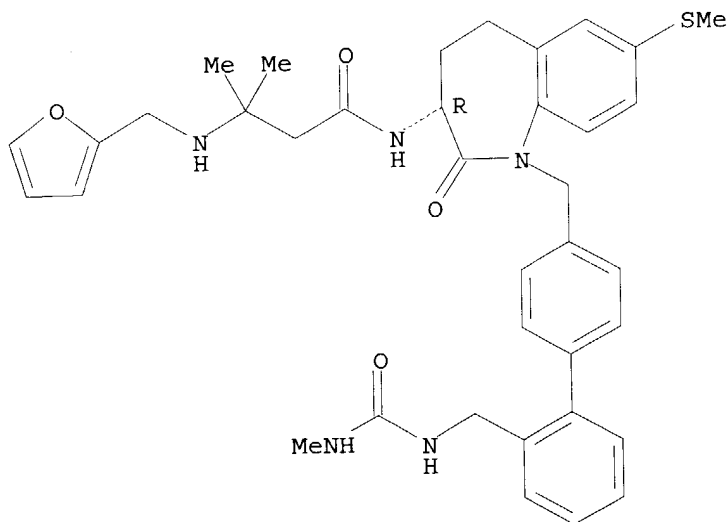
IT 169187-36-4P 169187-41-1P 169187-46-6P
 169187-51-3P 169187-56-8P 169187-61-5P
 169187-66-0P

(preparation of N-(oxobenzazepinyl)alkanamides as growth hormone release promoters)

RN 169187-36-4 USPATFULL

CN Butanamide, 3-[(2-furanylmethyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-1-[[2'-[[[(methylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

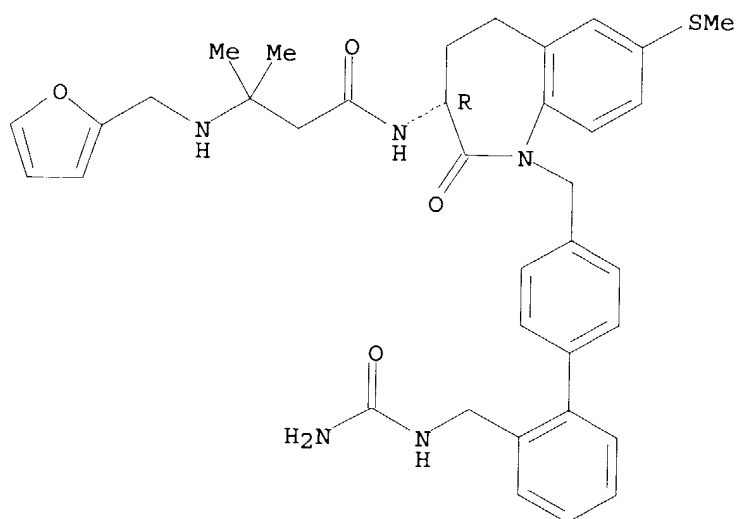


RN 169187-41-1 USPATFULL

CN Butanamide, N-[1-[[2'-[[[(aminocarbonyl)amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-

3-[(2-furanylmethyl)amino]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

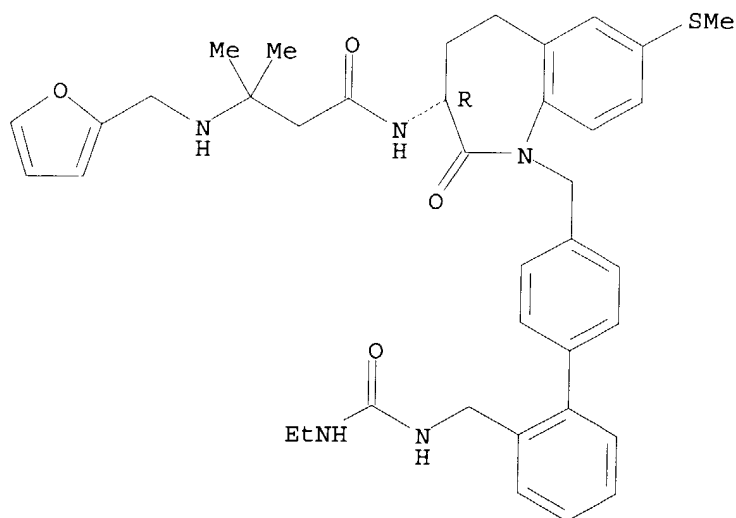
Absolute stereochemistry.



RN 169187-46-6 USPATFULL

CN Butanamide, N-[1-[[2'-[[[(ethylamino)carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2-furanylmethyl)amino]-3-methyl-, (R)- (9CI) (CA INDEX NAME)

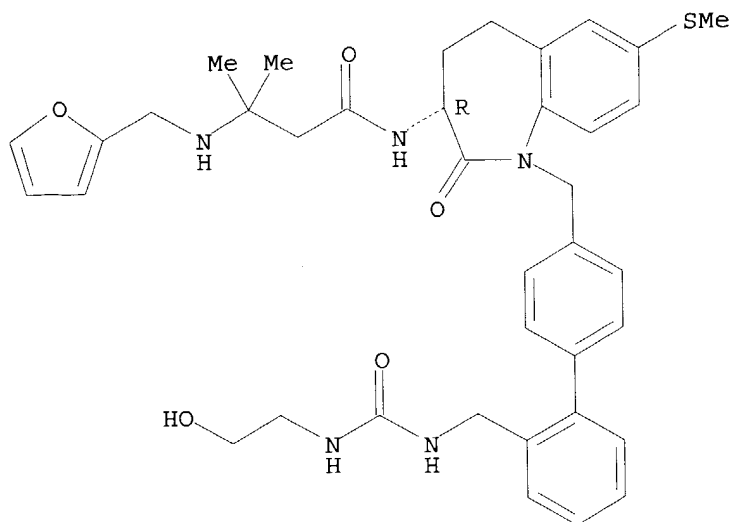
Absolute stereochemistry.



RN 169187-51-3 USPATFULL

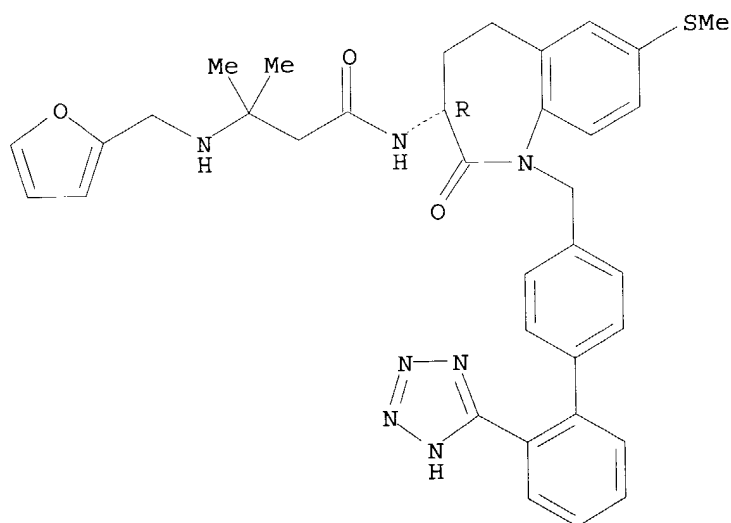
CN Butanamide, 3-[(2-furanylmethyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-1-[[2'-[[[(2-hydroxyethyl)amino]carbonyl]amino]methyl][1,1'-biphenyl]-4-yl]methyl]-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



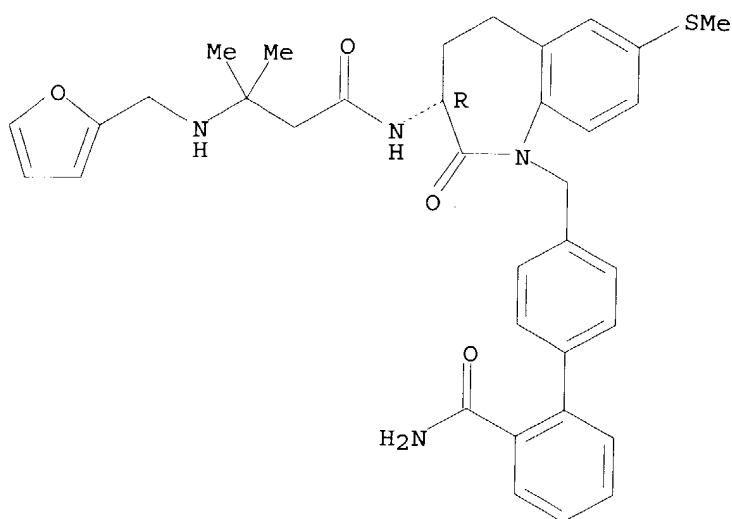
RN 169187-56-8 USPATFULL
 CN Butanamide, 3-[(2-furanylmethyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169187-61-5 USPATFULL
 CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[3-[[3-[(2-furanylmethyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl]-, (R)- (9CI) (CA INDEX NAME)

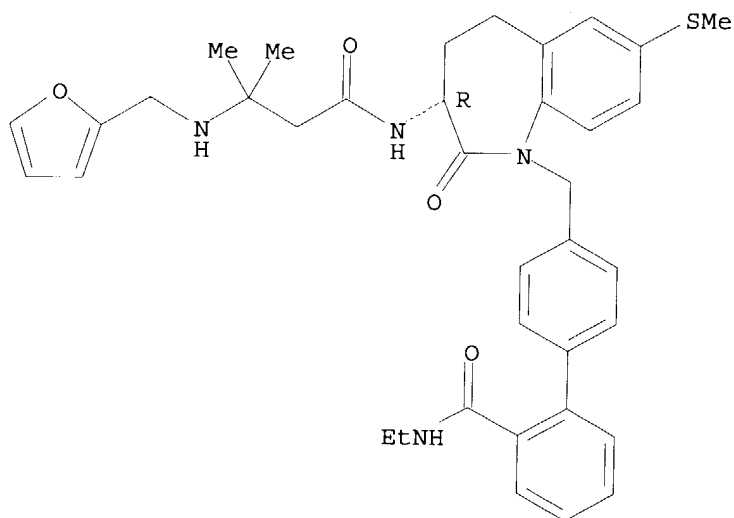
Absolute stereochemistry.



RN 169187-66-0 USPATFULL

CN [1,1'-Biphenyl]-2-carboxamide, N-ethyl-4'-[[3-[[3-[(2-furanylmethyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L52 ANSWER 24 OF 27 USPATFULL on STN

ACCESSION NUMBER: 94:110863 USPATFULL

TITLE: Benzo-fused lactams promote release of growth hormone

INVENTOR(S): Schoen, William R., Edison, NJ, United States

Wyvratt, Matthew J., Mountainside, NJ, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

NUMBER KIND DATE

searched by D. Arnold 571-272-2532

PATENT INFORMATION: US 5374721 19941220
 APPLICATION INFO.: US 1992-961008 19921014 (7)
 DOCUMENT TYPE: Utility
 FILE SEGMENT: Granted
 PRIMARY EXAMINER: Bond, Robert T.
 LEGAL REPRESENTATIVE: Rose, David L., DiPrima, Joseph F.
 NUMBER OF CLAIMS: 6
 EXEMPLARY CLAIM: 1
 LINE COUNT: 2322

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain novel compounds identified as benzo-fused lactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzo-fused lactams as the active ingredient thereof are also disclosed.

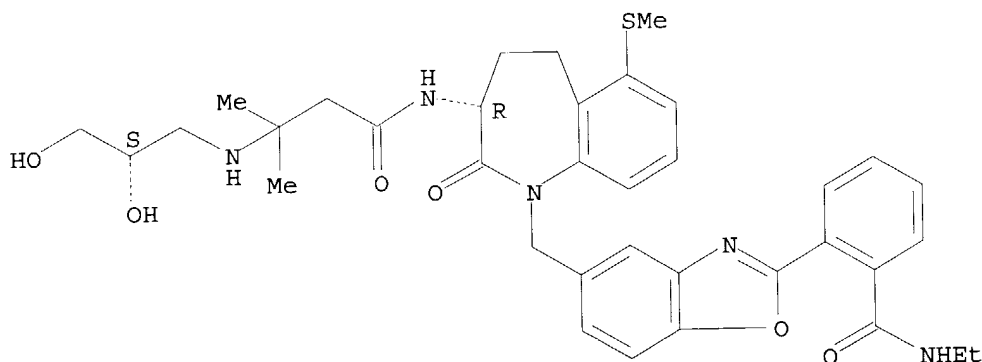
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 167822-74-4P 167822-97-1P
 (preparation of N-(N-heterocyclylbenzazepinyl)aminoalkanamides as growth hormone release promoters)

RN 167822-74-4 USPATFULL

CN Benzamide, 2-[5-[[3-[[3-[(2,3-dihydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-2,3,4,5-tetrahydro-6-(methylthio)-2-oxo-1H-1-benzazepin-1-yl]methyl]-2-benzoxazolyl]-N-ethyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

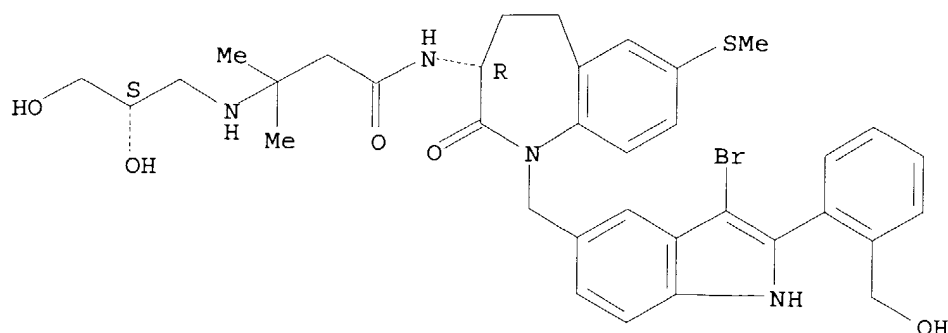
Absolute stereochemistry.



RN 167822-97-1 USPATFULL

CN Butanamide, N-[1-[[3-bromo-2-[2-(hydroxymethyl)phenyl]-1H-indol-5-yl]methyl]-2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1H-1-benzazepin-3-yl]-3-[(2,3-dihydroxypropyl)amino]-3-methyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L52 ANSWER 25 OF 27 USPATFULL on STN

ACCESSION NUMBER: 94:46974 USPATFULL

TITLE: N-biphenyl-3-amido substituted benzolactams stimulate growth hormone release

INVENTOR(S): Ok, Hyun O., Edison, NJ, United States

Schoen, William R., Edison, NJ, United States

Wyvratt, Matthew, Mountainside, NJ, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5317017		19940531
APPLICATION INFO.:	US 1992-954220		19920930 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Higel, Floyd D.		
LEGAL REPRESENTATIVE:	Rose, David L., DiPrima, Joseph F.		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1,7		
LINE COUNT:	2161		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain compounds identified as N-biphenyl-3-amido substituted benzolactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzolactams as the active ingredient thereof are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

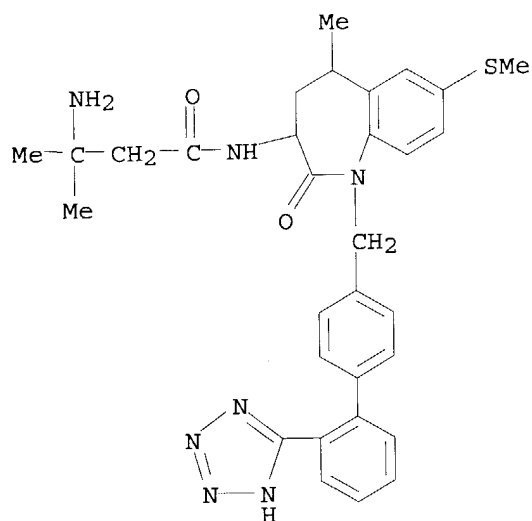
IT 158104-10-0 158104-11-1 158104-12-2

158104-21-3 158104-31-5 158104-42-8

(growth hormone release accelerator)

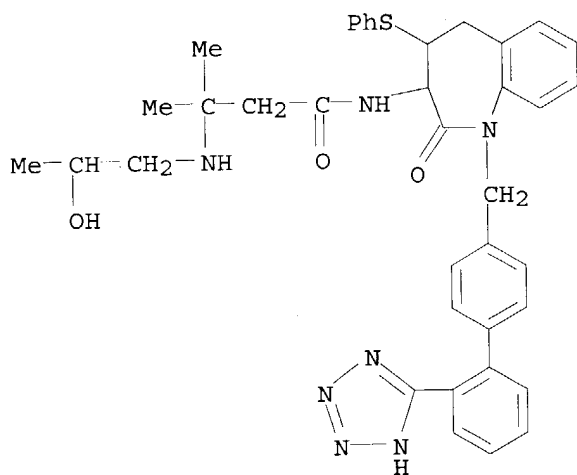
RN 158104-10-0 USPATFULL

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-5-methyl-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]- (9CI) (CA INDEX NAME)



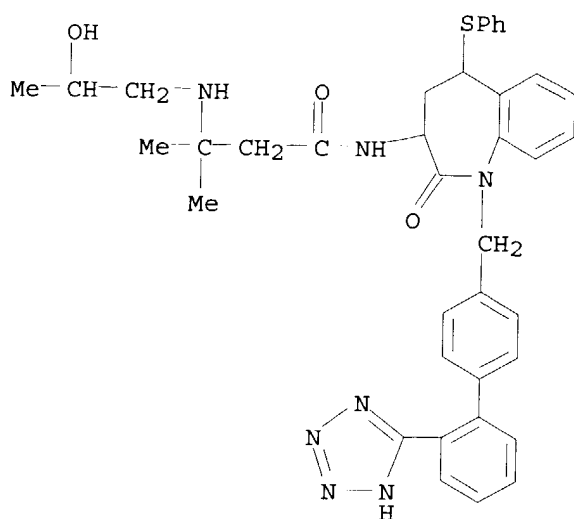
RN 158104-11-1 USPATFULL

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-4-(phenylthio)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]- (9CI) (CA INDEX NAME)



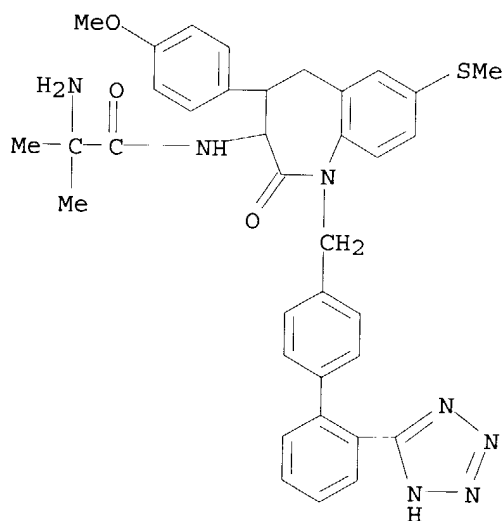
RN 158104-12-2 USPATFULL

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-2-oxo-5-(phenylthio)-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]- (9CI) (CA INDEX NAME)



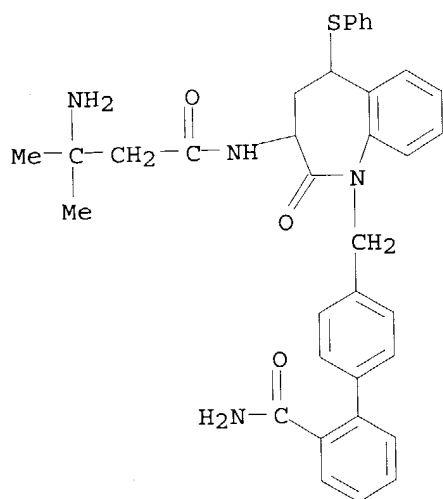
RN 158104-21-3 USPATFULL

CN Propanamide, 2-amino-2-methyl-N-[2,3,4,5-tetrahydro-4-(4-methoxyphenyl)-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]- (9CI) (CA INDEX NAME)



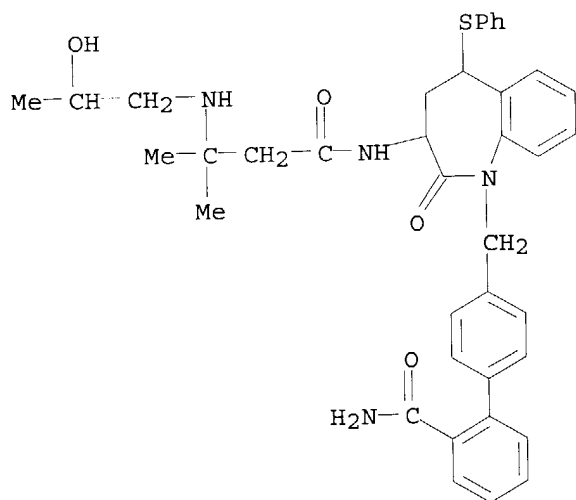
RN 158104-31-5 USPATFULL

CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[3-[(3-amino-3-methyl-1-oxobutyl)amino]-2,3,4,5-tetrahydro-2-oxo-5-(phenylthio)-1H-1-benzazepin-1-yl]methyl]- (9CI) (CA INDEX NAME)



RN 158104-42-8 USPATFULL

CN [1,1'-Biphenyl]-2-carboxamide, 4'-[[2,3,4,5-tetrahydro-3-[[3-[(2-hydroxypropyl)amino]-3-methyl-1-oxobutyl]amino]-2-oxo-5-(phenylthio)-1H-1-benzazepin-1-yl]methyl]- (9CI) (CA INDEX NAME)



L52 ANSWER 26 OF 27 USPATFULL on STN

ACCESSION NUMBER: 94:40056 USPATFULL

TITLE: Benzo-fused lactams that promote the release of growth hormone

INVENTOR(S): Fisher, Michael H., Ringoes, NJ, United States
 Schoen, William R., Edison, NJ, United States
 Wyvratt, Matthew J., Mountainside, NJ, United States
 DeVita, Robert J., Westfield, NJ, United States

PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

NUMBER	KIND	DATE
--------	------	------

PATENT INFORMATION: US 5310737 19940510
 APPLICATION INFO.: US 1993-12190 19930202 (8)
 RELATED APPLN. INFO.: Division of Ser. No. US 1992-839742, filed on 28 Feb 1992, now patented, Pat. No. US 5206235 which is a continuation-in-part of Ser. No. US 1991-673695, filed on 20 Mar 1991, now abandoned
 DOCUMENT TYPE: Utility
 FILE SEGMENT: Granted
 PRIMARY EXAMINER: Shah, Mukund J.
 ASSISTANT EXAMINER: Sripada, Pavanaram R.
 LEGAL REPRESENTATIVE: Rose, David L., DiPrima, Joseph F.
 NUMBER OF CLAIMS: 9
 EXEMPLARY CLAIM: 1
 LINE COUNT: 6705

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain novel compounds identified as benzo-fused lactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzo-fused lactams as the active ingredient thereof are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

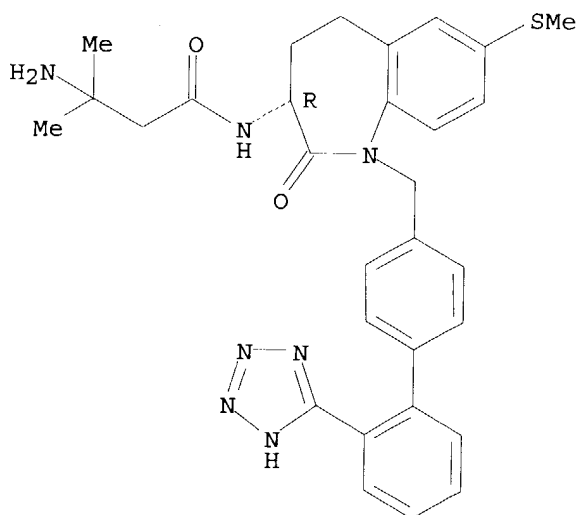
IT 145455-70-5P 145455-71-6P 145455-72-7P
 145455-73-8P 145552-97-2P 145552-98-3P

(preparation of, as growth hormone release promoter)

RN 145455-70-5 USPTFULL

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA INDEX NAME)

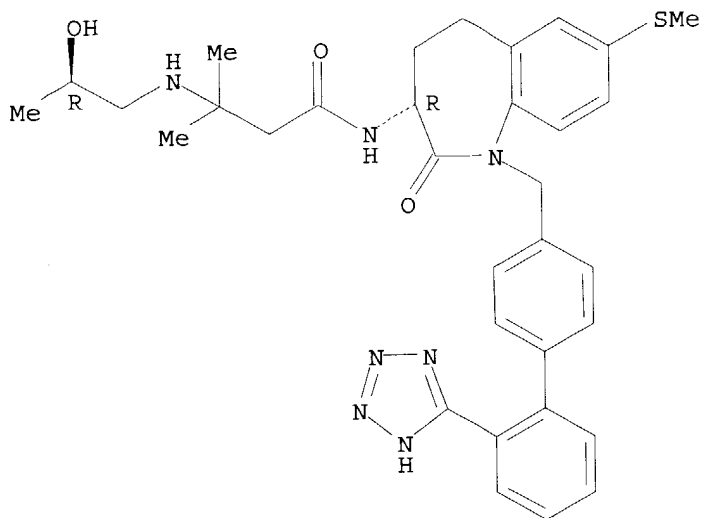
Absolute stereochemistry.



RN 145455-71-6 USPTFULL

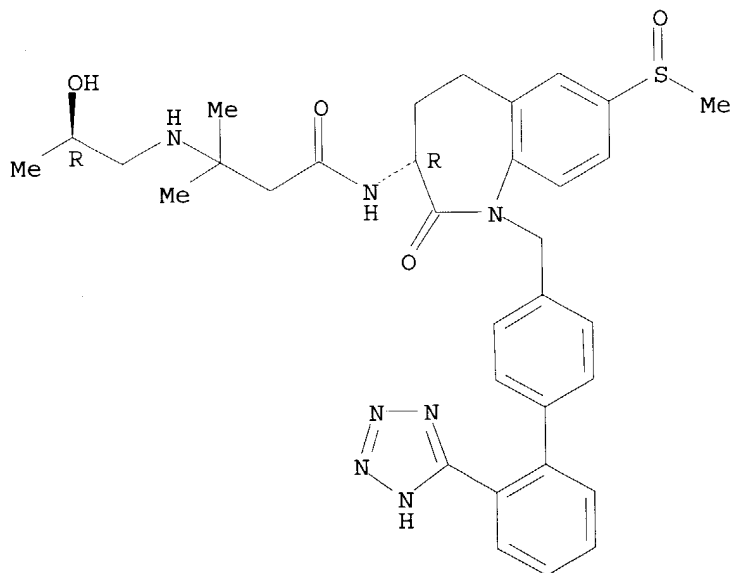
CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



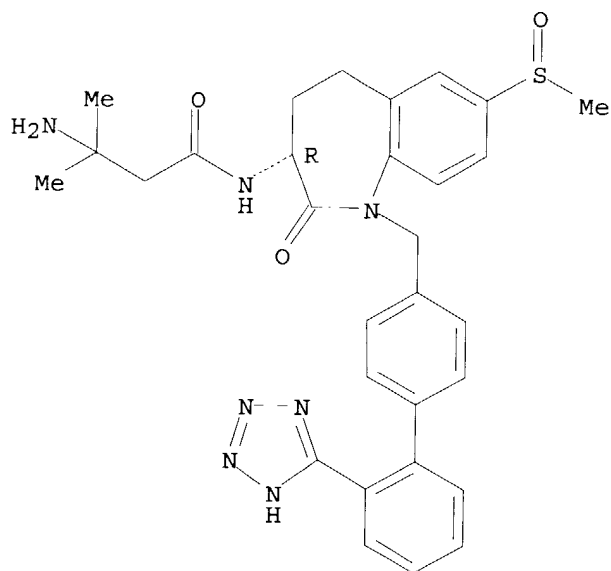
RN 145455-72-7 USPTAFULL
 CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, [3R-[3R*(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



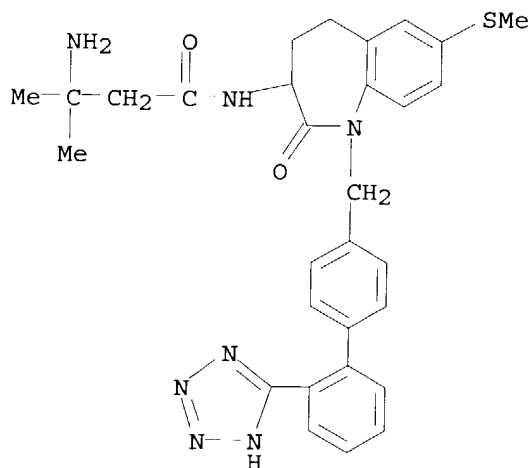
RN 145455-73-8 USPTAFULL
 CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 145552-97-2 USPATFULL

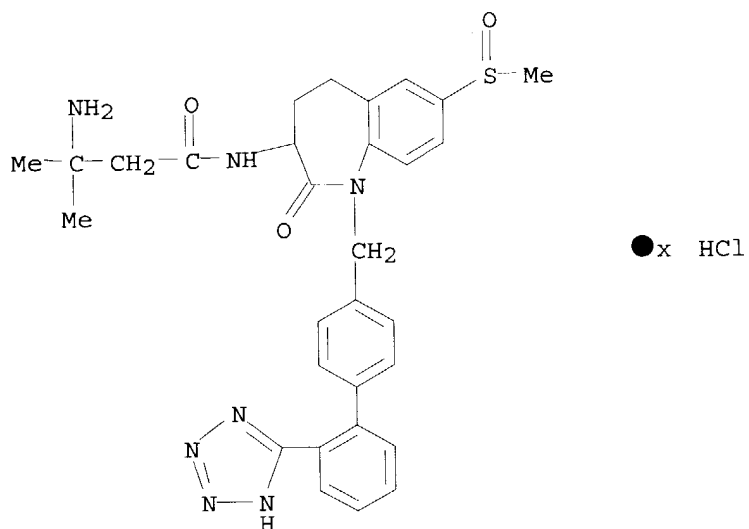
CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 145552-98-3 USPATFULL

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, hydrochloride (9CI) (CA INDEX NAME)



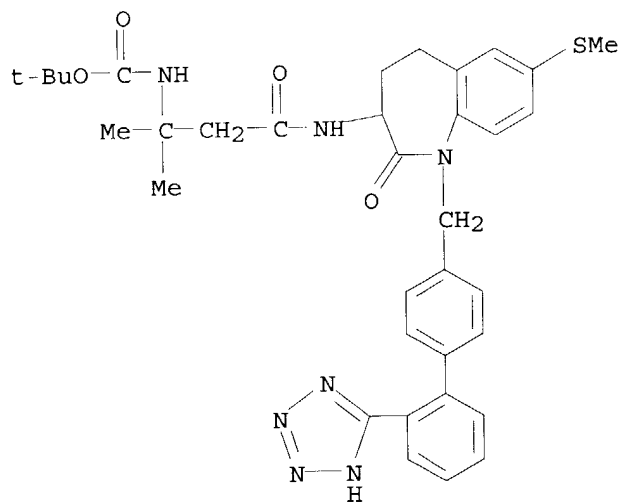
IT 146429-18-7P 146429-19-8P

(preparation of, as intermediate for growth hormone release promoter)

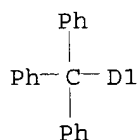
RN 146429-18-7 USPATFULL

CN Carbamic acid, [1,1-dimethyl-3-oxo-3-[[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-[(triphenylmethyl)-1H(or 2H)-tetrazol-5-yl][1,1'-biphenyl]-4-yl)methyl]-1H-1-benzazepin-3-yl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

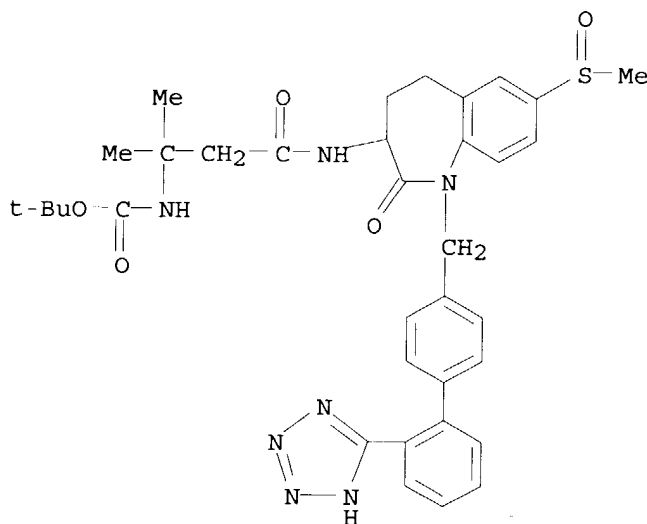


PAGE 2-A

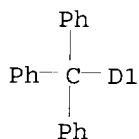


RN 146429-19-8 USPATFULL
 CN Carbamic acid, [1,1-dimethyl-3-oxo-3-[[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-[(triphenylmethyl)-1H(or 2H)-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L52 ANSWER 27 OF 27 USPATFULL on STN
 ACCESSION NUMBER: 93:33488 USPATFULL
 TITLE: Benzo-fused lactams that promote the release of growth hormone
 INVENTOR(S): Fisher, Michael H., Ringoes, NJ, United States
 Schoen, William R., Edison, NJ, United States
 Wyvratt, Matthew J., Mountainside, NJ, United States
 DeVita, Robert J., Westfield, NJ, United States
 PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5206235		19930427
APPLICATION INFO.:	US 1992-839742		19920228 (7)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1991-673695, filed on 20 Mar 1991, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Berch, Mark L.		

LEGAL REPRESENTATIVE: Rose, David L., DiPrima, Joseph F.
 NUMBER OF CLAIMS: 8
 EXEMPLARY CLAIM: 1
 LINE COUNT: 6831

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed certain novel compounds identified as benzo-fused lactams which promote the release of growth hormone in humans and animals. This property can be utilized to promote the growth of food animals to render the production of edible meat products more efficient, and in humans, to increase the stature of those afflicted with a lack of a normal secretion of natural growth hormone. Growth promoting compositions containing such benzo-fused lactams as the active ingredient thereof are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

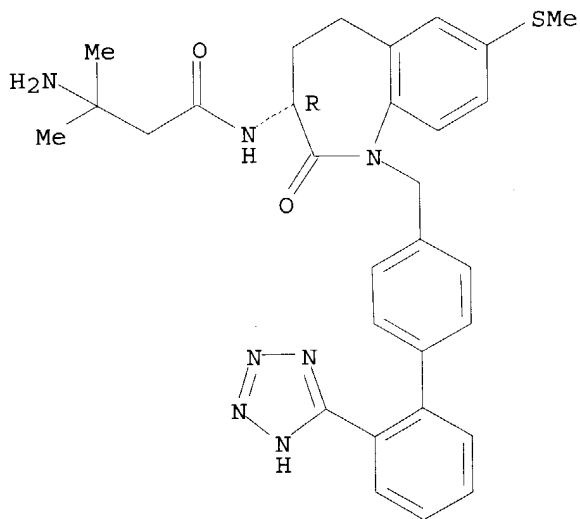
IT 145455-70-5P 145455-71-6P 145455-72-7P
 145455-73-8P 145552-97-2P 145552-98-3P

(preparation of, as growth hormone release promoter)

RN 145455-70-5 USPATFULL

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, (R)- (9CI) (CA INDEX NAME)

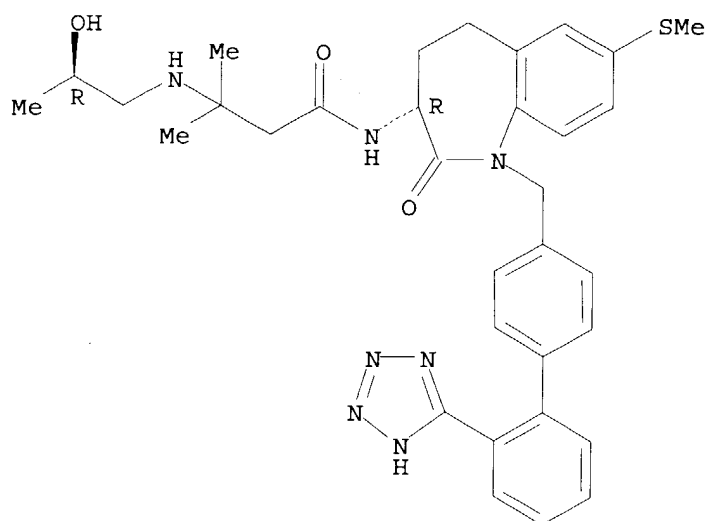
Absolute stereochemistry.



RN 145455-71-6 USPATFULL

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

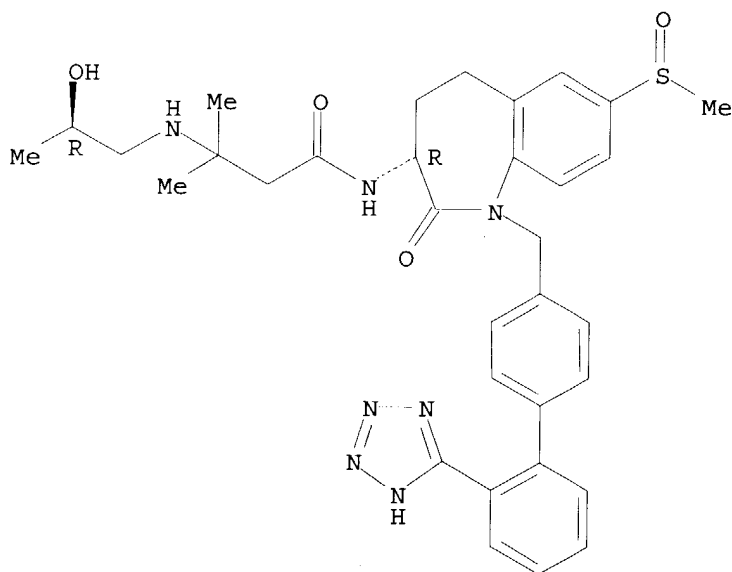
Absolute stereochemistry.



RN 145455-72-7 USPATFULL

CN Butanamide, 3-[(2-hydroxypropyl)amino]-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, [3R-[3R*(R*)]]- (9CI) (CA INDEX NAME)

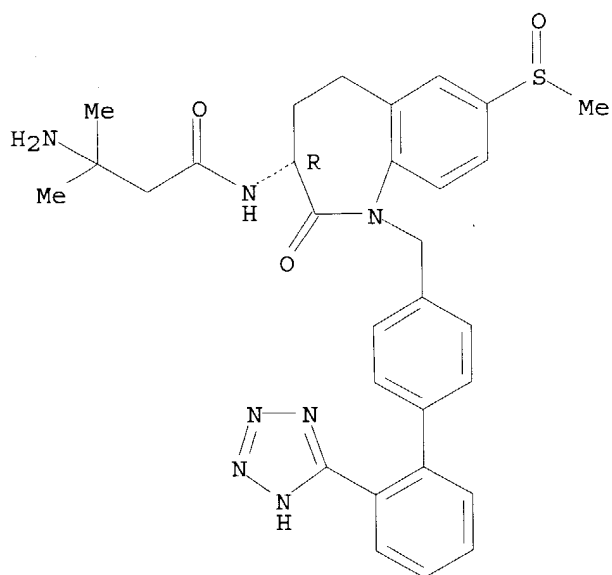
Absolute stereochemistry.



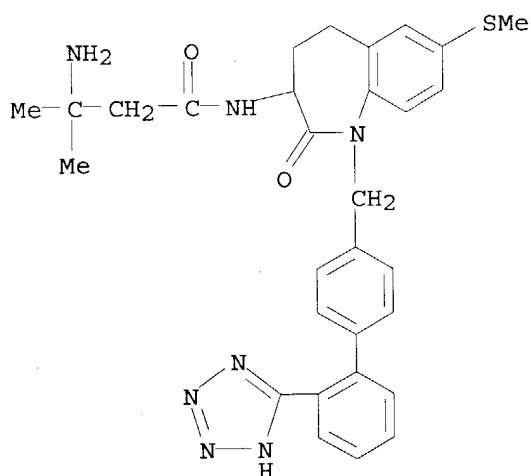
RN 145455-73-8 USPATFULL

CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

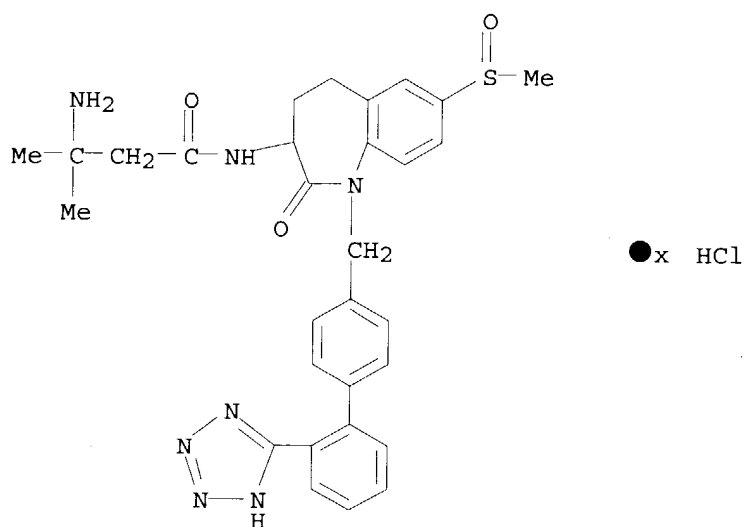


RN 145552-97-2 USPATFULL
 CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 145552-98-3 USPATFULL
 CN Butanamide, 3-amino-3-methyl-N-[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]-, hydrochloride (9CI) (CA INDEX NAME)



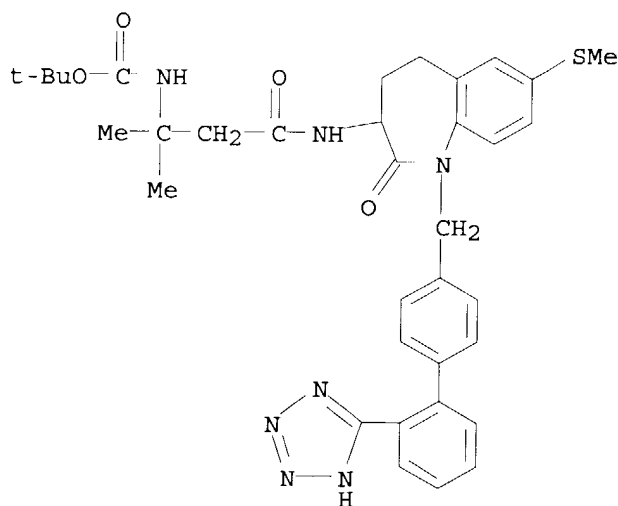
IT 146429-18-7P 146429-19-8P

(preparation of, as intermediate for growth hormone release promoter)

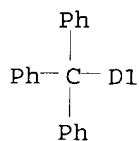
RN 146429-18-7 USPTFULL

CN Carbamic acid, [1,1-dimethyl-3-oxo-3-[[2,3,4,5-tetrahydro-7-(methylthio)-2-oxo-1-[[2'-[(triphenylmethyl)-1H(or 2H)-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

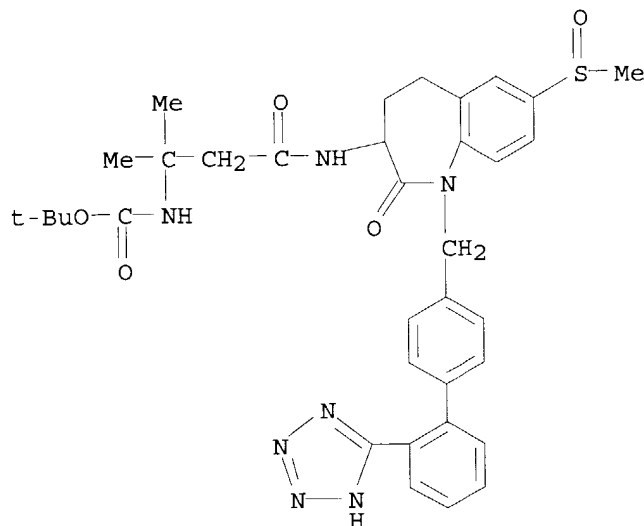


PAGE 2-A

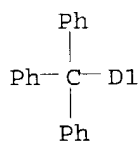


RN 146429-19-8 USPATFULL
 CN Carbamic acid, [1,1-dimethyl-3-oxo-3-[[2,3,4,5-tetrahydro-7-(methylsulfinyl)-2-oxo-1-[[2'-[(triphenylmethyl)-1H(or 2H)-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-1H-1-benzazepin-3-yl]amino]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



=>
 => file stnguide

FILE 'STNGUIDE' ENTERED AT 11:46:12 ON 27 NOV 2004
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
 COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Nov 19, 2004 (20041119/UP).

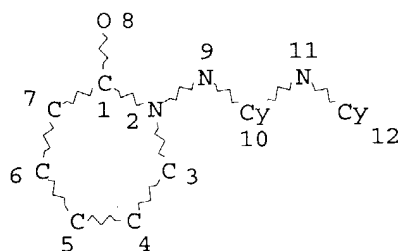
=> => d que 139
 L1 (156603)SEA FILE=REGISTRY ABB=ON PLU=ON NC6/ESS
 L2 STR



```
STEREO ATTRIBUTES: NONE
L3          3855 SEA FILE=REGISTRY SUB=L1 SSS FUL L2
L16         STR
```



STEREO ATTRIBUTES: NONE
L18 STR



NODE ATTRIBUTES:

NSPEC IS RC AT 9
 NSPEC IS RC AT 11
 CONNECT IS E1 RC AT 8
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L21 3042 SEA FILE=REGISTRY SUB=L3 SSS FUL (L16 OR L18)
 L22 434 SEA FILE=REGISTRY ABB=ON PLU=ON L21 AND S/ELS
 L29 58 SEA FILE=HCAPLUS ABB=ON PLU=ON L22
 L38 15819 SEA FILE=HCAPLUS ABB=ON PLU=ON ?METALLOPROTEAS? OR MMP?
 L39 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L38 AND L29

=>